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UNITED STATES ATOMIC ENERGY COMMISSION

PROGRESS REPORT ON METABOLISM OF FISSION PRODUCTS
FOR PERIOD ENDING OCTOBER 15, 1943

by

Roy Overstreet
Louis Jacobson
Harvey Fisher
Kenneth Scott
Dorothy Axelrod

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ABSTRACT

Part A. Unseparated Fission Products: Unseparated fission products have been iso-lated from 18 pounds of neutron bombarded $UO_2(NO_3)_2 \cdot 6H_2O$ free from carrier and con-taining less than .03 micrograms of Uranium per microcurie of activity. The final solution was assayed for its content of Strontium, Yttrium + Praseodymium, Zirconium, Columbium, Ruthenium, Tellurium, Cesium, Barium, Cerium, and UX_1. Tracer studies were done on a large group of rats which received the prepared solution by intramuscular, intraperitoneal, intrapulmonary, and oral routes of administration. The time intervals ranged from one to sixty-four days. The skeleton was the chief point of deposition for the absorbed radioactive mixture for all four routes of administration. Considerable and prolonged retention oc-curred in the lungs following intrapulmonary administration. From 3 to 5% was absorbed from the digestive tract.

Excretion was slow and the digestive tract was the chief channel of elimination. Approximately 50% of the activity was excreted over the sixty-four day period following intraperitoneal and intramuscular injection.

Part B. Radio-Ruthenium ($Ru^{>105}$): A carrier free purified preparation of Ru^{105} has been isolated as a solution of $RuCl_4$ and tracer studies comparable to those for the fission mixture completed. $Ru^{>105}$ was found to be rather widely distributed throughout the body and the greatest degree of selective localization took place in the kidney which was con-siderably less than the degree of deposition and retention in bone for the alkaline earths, rare earths, Zirconium, Columbium, and the fission mixture. Excretion was much more rapid than for the above listed substances and by sixty-four days in the intraperitoneal and intramuscular group less than 15% of the administered $Ru^{>105}$ was retained. Roughly 2/5ths was eliminated by way of the kidneys and 3/5ths by the digestive tract over the sixty-four day interval. No significant absorption took place by way of the digestive tract. Consider-able retention of $Ru^{>105}$ took place in the lungs following intrapulmonary administration of the solution of $RuCl_4$. The distribution of the absorbed fraction was similar to that noted in the intraperitoneal and intramuscular studies.

Part C. Neptunium ($Np^{238,239}$): A mixture of Np^{238} and Np^{239}, free from radioactive con-taminents and inert hold-back carriers, was isolated from a Uranium metal target which had been bombarded by 16Mev deuterons. Tracer studies, which included the intraper-itoneal, intrapulmonary, and oral routes of administration, were carried out over a period of 8 days. The metabolic behaviour of Neptunium was found to resemble that of Yttrium more closely than any of the other fission products studied thus far. The pulmonary re-tention following intrapulmonary administration was considerably less than for the rare earths, Zirconium, Columbium, Ruthenium and fission mixture. Excretion was more rapid than that noted for the substances listed above with the exception of Ruthenium. The amount eliminated during the 8 day period of the experiments was almost equally divided between digestive tract and kidneys. No significant absorption by way of the digestive tract took place.

Part D. Radio-Autographic Studies: A large series of radio-autographs have been prepared from the lungs of the rats which had received the fission mixture, Ruthenium and Neptunium by intrapulmonary administration. Photo-micrographs of representative lung sections and their corresponding radio-autographs are included in the report. In the large series of radio-autographs prepared no significant deposition was noted in the bronchi, lymphoid tissue, and blood vessels. In all of the radio-autographs it was found that the radioactivity was distributed widely throughout the alveolar structure of the lungs. Frequently a tendency for the alveolar pattern of the sections to be duplicated on the radio-autograph was observed.

Part A

UNSEPARATED FISSION PRODUCTS

By Roy Overstreet, Louis Jacobson, Harvey Fisher, and Kenneth Scott

1. Preparation Without Carrier and Assay

Assay of Fission Products

An aliquot of the fission-products solution was diluted to 45cc and 100 mgs each of Strontium, Yttrium, Zirconium, Columbium, Ruthenium, Tellurium, Cesium, Barium, Lanthanum, Cerium and Thorium were added. The solution was made basic to litmus with concentrated Ammonium Hydroxide (carbonate free), and then 10cc was added in excess. The resulting precipitate was centrifuged down and dissolved in 2cc of concentrated HCl. This solution was diluted to 50cc and treated with Ammonia as before. The combined supernatant fluids were acidified and set aside for the Barium, Strontium, and Cesium determinations.

The Ammonium Hydroxide precipitate was dissolved in HCl and diluted to 3N in H^+. The total volume was 120cc. Two cc of 85% phosphoric acid solution was added and the mixture was boiled for thirty minutes. The precipitate of Zirconium and Columbium was centrifuged down and washed with 5% Ammonium Nitrate. The washings were combined with the first supernatant liquid and set aside for the determination of Ruthenium, Tellurium and the rare earths.

The washed precipitate of Zirconium and Columbium was discarded, owing to the development of a more suitable method for the determination of these elements.

Ruthenium and Tellurium: The Ruthenium and Tellurium were precipitated as the sulfides from the phosphate filtrate. The sulfides were brought into solution and reprecipitated in the presence of Yttrium, Lanthanum, Cerium, Thorium, Barium, Strontium, Cesium, and Zirconium hold-back carriers. Tellurium was separated as the metal from Ruthenium by means of SO_2. Ruthenium was then precipitated as the sulfide. Ruthenium hold-back carrier was added to the Tellurium fraction and Tellurium hold-back carrier was added to the Ruthenium fraction and the two elements were again separated.

Rare Earths: The rare-earths were precipitated as the fluorides from the original Ruthenium and Tellurium sulfide filtrate. The precipitate was decomposed and the rare-earths were precipitated as the hydroxides. Columbium, Zirconium, Cesium, Ruthenium, Tellurium, Cerium and Strontium hold-back carriers were added and the rare earths were carried through above cycle once more. Cerium and Thorium were separated as the iodates, redissolved, and again precipitated as the iodates in the presence of Yttrium and Lanthanum hold-back carriers. The Cerium was reduced and the Thorium was precipitated as the iodate.

Cerium hold-back carrier was added to the Thorium fraction and Thorium hold-back carrier was added to the Cerium fraction and the two elements were again separated.

Inert Cerium and Thorium was added to the filtrate from the original iodate precipitate. The Cerium and Thorium were then precipitated as the iodate and Yttrium and Lanthanum were separated from the filtrate as the hydroxides.

Barium and Strontium: The Barium and Strontium were precipitated from the Barium, Strontium, and Cesium fraction with Ammonium Carbonate. The Ammonium Carbonate precipitate was dissolved and hold-back carriers for the other fission components were added. The Barium and Strontium Carbonates were separated as before. Barium was separated from Strontium by precipitation of the chloride from saturated HCl solution. Inert Barium was added to the Strontium fraction and inert Strontium was added to the Barium fraction and the separation was repeated.

Cesium: Cesium was separated from filtrate of the Barium and Strontium Carbonate precipitate as the perchlorate. The Cesium perchlorate was dissolved in water. Inert carriers for the other fission components were added. The solution was treated with Ammonium Carbonate and $CsClO_4$ was precipitated from the filtrate.

Zirconium and Columbium: A fresh aliquot of the original fission products solution was taken. One hundred mgs each of Strontium, Barium, Cesium, Ruthenium, Tellurium, and Zirconium were added. The solution was treated with Ammonium Hydroxide and the precipitate was centrifuged out and dissolved in HCl. Strontium, Barium, and Cesium hold-back carriers were added and the solution was again made Ammoniacal. The precipitate was centrifuged out and dissolved in HNO_3. One hundred mgs of Columbium was added and the solution was adjusted to 5N HNO_3 in a volume of 20cc. An equal volume of 0.35N KIO_3 was added and the resulting iodate precipitate was centrifuged down. The precipitate was decomposed with concentrated HCl and 100 mgs each of Thorium, Cerium, Yttrium, and Lanthanum were added. The rare earths were then precipitated as the fluorides and discarded. The filtrate was evaporated down and fumed with concentrated H_2SO_4. The solution was diluted and inert Thorium, Cerium, Yttrium, and Lanthanum were added. The rare earths were again precipitated as the fluorides and discarded. The filtrate from the fluoride precipitate was fumed with H_2SO_4. The solution was diluted and the Zirconium and Columbium were precipitated with NH_4OH. The two elements were separated by means of a carbonate fission. Columbium was precipitated from the carbonate filtrate with SO_2. Inert Columbium was added to the Zirconium fraction and inert Zirconium was added to the Columbium fraction and the two elements were separated as before.

Determination of Percentage Activity of Fission Components

The Zirconium, Columbium, Cerium, Thorium, and Yttrium + Lanthanum fractions were ignited to the oxides. The Strontium and Barium fractions were ignited as the sulfates. The Cesium, determined as the perchlorate, was heated to 325°C to remove excess perchloric acid. The Tellurium, which was isolated as the metal, was dried at 100°C. The Ruthenium was finally ignited as the sulfide. Owing to the indeterminant composition of the Ruthenium

Oxide, exactly 100 mgs of Ruthenium was converted to the sulfide and ignited under identical conditions to serve as a standard in the calculation of the Ruthenium recovery. In each case, the various fractions were carefully weighed and the percentage recovery calculated.

For the measurement of the activities, the samples were finely ground and uniformly spread on cellophane dishes. The dishes were mounted under the electroscope on a cellophane sheet. The activities were thus measured and corrected to 100% recovery. All activities were measured after sufficient time had elapsed for the Lanthanum to decay out of the Yttrium + Lanthanum fraction and for the Barium fraction to reach equilibrium with the Lanthanum daughter. Aluminum absorption curves were run on each fraction to enable the extrapolation to zero filter thickness. In preparing the curves, account was taken of the mass absorption of the sample and of the air gap plus window thickness. By means of the absorption curves, the percentage activity of each fraction was calculated for both 11 mgs/cm^2 and zero filter thicknesses. The values for April 9, 1943 (81 days after bombardment) are presented in the following table.

The low value for Ruthenium was probably due to loss by volatilization during the preparation of the fission mixture.

Table 1

ACTIVITIES OF FRACTIONS OF FISSION-PRODUCTS SOLUTION
APRIL 9, 1943

FRACTION	% OF TOTAL ACTIVITY EXCLUSIVE OF UX_1, UX_2 ZERO FILTER THICKNESS	% OF TOTAL ACTIVITY EXCLUSIVE OF UX_1, UX_2 11 mgs/cm^2 FILTER THICKNESS
Sr	10.9	16.4
Y+Pr	17.0	25.6
Zr	24.9	20.4
Cb	9.10	1.65
Ru	0.54	0.25
Te	1.48	0.48
Cs	0.44	0.50
Ba+La	5.68	7.93
Ce	30.1	27.1
Th(UX_1, UX_2)	2.47 (of total)	2.14 (of total)

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2. Tracer Studies

The purified Uranium free unseparated fission products after 87 days of cooling were injected in an isotonic solution of Sodium Chloride at a pH of 2.5 into the following groups of three rats each: Four intraperitoneal, three intramuscular, three oral, and three intrapulmonary. Each animal received from two to five microcuries of the fission mixture. The intraperitoneal animals were sacrificed at one, four, sixteen, and sixty-four days. The intramuscular, oral, and intrapulmonary were sacrificed at four, sixteen, and sixty-four days. The excreta was collected for the intraperitoneal, intramuscular, and oral groups at daily intervals. Frequently it was necessary to pool the urine and feces for many of the groups for two successive days due to the large number of samples involved in experiments of this magnitude. The tissues were removed, ashed and measured as has been described in section C Part 2 of Report #CH 498. Before the samples were ashed known amounts of the fission mixture were admixed with inert tissues and ashed overnight at 500°C. No detectable loss of activity from volatilization was observed although considerable loss of the small amount of Ru $^{>105}$ present (0.5%) probably occurred.

Results

In general it may be said that the results of this much more extensive series of studies (Tables 2-6) confirms the results obtained in the earlier and far more incomplete experiments (CH498). The rather striking differences between the deposition of the fission mixture in the abdominal organs of the intraperitoneal group (Tables 2,3) as compared to the intramuscular animals (Table 4) was presumably due to the surface contamination of these tissues. It is of interest to note in passing that the spleen does not show any very marked tendency to accumulate a high proportion of the injected material. An interesting observation was that in the intraperitoneal animals the amount taken up by the lungs was sometimes ten to twenty times greater than the corresponding value for the intramuscular animal. This phenomenon occurred in a highly irregular fashion, frequently only one of each of the three animals would show this effect. It will be recalled that a similar phenomenon occurred in the Cerium experiments and also has been noted with Zirconium. An adequate explanation cannot be offered at present for this most unusual finding. The excretion in both the intraperitoneal and intramuscular groups revealed no striking differences in the rates of elimination (Figures 1-4). It can be seen that the combined rates of urinary and fecal excretion falls within a month to a rate of less than 1% per day.

The oral uptake (Table 5) was found to be somewhat greater than in the preliminary experiments in Report #CH 498, but the distribution indicated that practically all of the absorbed activity was deposited in the skeleton. The measured values from some of the smaller tissues such as the heart were not accurate due to the weak activities present. A more accurate index of the amount of activity present in the soft tissues can be gained by the balance values which on a per gram basis indicated an activity of from 1/90th to 1/200th of that of the bone. From the amount absorbed by way of the digestive tract together with the distribution of the absorbed fraction it is apparent that most of the activity in the body was Strontium and Barium.

Table 2

THE DISTRIBUTION OF CARRIER FREE UNSEPARATED FISSION PRODUCTS
FOLLOWING INTRAPERITONEAL INJECTION

	ONE DAY		FOUR DAYS	
	%UPTAKE PER GRAM	%UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN
Heart	.051	.06	.030	.03
Liver	1.628	19.10	1.697	20.37
Kidney	.462	1.44	.531	1.30
Testes	.140	.61	.126	.55
Spleen	1.344	1.43	.538	.55
Muscle[1]	.013	1.91	.009	1.22
Skin[2]	.047	1.97	.058	2.48
Stomach	.438	1.53	.193	.84
Sm. Intestine	.377	4.88	.316	3.05
Lg. Intestine	.439	.26	.060	.11
Bone[3]	1.353	33.09	1.677	39.22
Lung	.088	.22	.343	.77
Brain	.016	.03	.007	.008
Belly Muscle[4]	.104	---	.407	---
Blood[5]	.041	1.08	.015	.38
Adrenals	.282	.02	.247	.02
Lymph Nodes	.054	---	.052	---
Tail Fat	---	---	---	---
Feces[6]	.470	---	.402	---
Balance[7]		23.93		15.30
Total Urine		5.90		2.55
Total Feces		7.10		13.70
Total Recovery		99.61		98.37

1. Muscle was calculated on basis of 45% of total body weight.
2. Skin was calculated on basis of 42 grams.
3. Measured value for entire skeleton.
4. A sample of muscle from the anterior abdominal wall at the site of injection.
5. Blood was calculated on basis of 8% of total body weight.
6. Sample of feces removed from large intestines when animals were sacrificed.
7. Balance was measured value for remaining carcass less the skeleton but including blood, muscle and skin.

Table 3

THE DISTRIBUTION OF CARRIER FREE UNSEPARATED FISSION PRODUCTS
FOLLOWING INTRAPERITONEAL INJECTION (CONTINUED)

	SIXTEEN DAYS		SIXTY-FOUR DAYS	
	% UPTAKE PER GRAM	% UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN
Heart	.033	.04	.027	.03
Liver	.797	9.06	.227	2.99
Kidney	.406	1.02	.252	.65
Testes	.072	.27	.082	.30
Spleen	.713	1.21	.519	.60
Muscle[1]	.011	1.40	.007	1.00
Skin[2]	.042	1.78	.038	1.60
Stomach	.134	.46	.209	.73
Sm. Intestine	.727	7.23	.185	2.41
Lg. Intestine	.142	.05	.198	.10
Bone[3]	1.607	39.80	1.093	39.66
Lung	.718	1.67	.175	.552
Brain	.008	.012	.008	.011
Belly Muscle[4]	.181	---	.105	---
Blood[5]	.008	.18	.003	.08
Adrenals	.189	.01	.106	.005
Lymph Nodes	.038	---	.066	---
Tail Fat	.061	---	.063	---
Feces[6]	.071	---	.013	---
Balance[7]		14.93		7.15
Total Urine		6.95		4.73
Total Feces		23.01		47.14
Total Recovery		105.72		107.06

1. Muscle was calculated on basis of 45% of total body weight.
2. Skin was calculated on basis of 42 grams.
3. Measured value for entire skeleton.
4. A sample of muscle from the anterior abdominal wall at the site of injection.
5. Blood was calculated on basis of 8% of total body weight.
6. Sample of feces removed from large intestines when animals were sacrificed.
7. Balance was measured value for remaining carcass less the skeleton but including blood, muscle and skin.

Table 4

THE DISTRIBUTION OF CARRIER FREE UNSEPARATED FISSION PRODUCTS
FOLLOWING INTRAMUSCULAR INJECTION

	FOUR DAYS		SIXTEEN DAYS		SIXTY-FOUR DAYS	
	%UPTAKE PER GRAM	%UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN
Heart	.037	.04	.031	.04	.029	.03
Liver	1.16	10.60	.44	5.69	.12	1.51
Kidney	.48	1.13	.23	.62	.21	.61
Testes	.022	.08	.026	.094	.036	.14
Spleen	.096	.10	.10	.16	.10	.14
Muscle[1]	.010	1.52	.009	1.53	.007	1.11
Skin[2]	.085	3.58	.038	1.62	.032	1.33
Stomach	.050	.17	.018	.06	.014	.05
Sm. Intestine	.035	.26	.016	.20	.012	.12
Lg. Intestine	.036	.024	.024	.023	.024	.016
Bone[3]	1.72	37.07	1.47	38.02	1.27	41.79
Lungs	.057	.12	.051	.12	.048	.087
Brain	.006	.008	.006	.01	.007	.01
Blood[4]	.017	.37	.008	.23	.003	.09
Adrenals	.023	.0015	.037	.003	.072	.004
Lymph Nodes	.063		.056		.064	
Feces[5]	.965		.058		.025	
Unab. in Left Leg[6]		33.22		27.78		17.27
Balance[7]		9.90		4.00		5.58
Total Urine		3.48		7.53		9.99
Total Feces		12.73		27.60		45.07
Total Recovery		108.93		111.95		122.42

1. Muscle was calculated on basis of 45% of total body weight.
2. Skin was calculated on basis of 42 grams.
3. Measured value for entire skeleton.
4. Blood was calculated on basis of 8% of total body weight.
5. Sample of feces removed from large intestines when animals were sacrificed.
6. Unabsorbed fraction in left leg.
7. Balance was measured value for remaining carcass less the skeleton but including blood, muscle and skin.
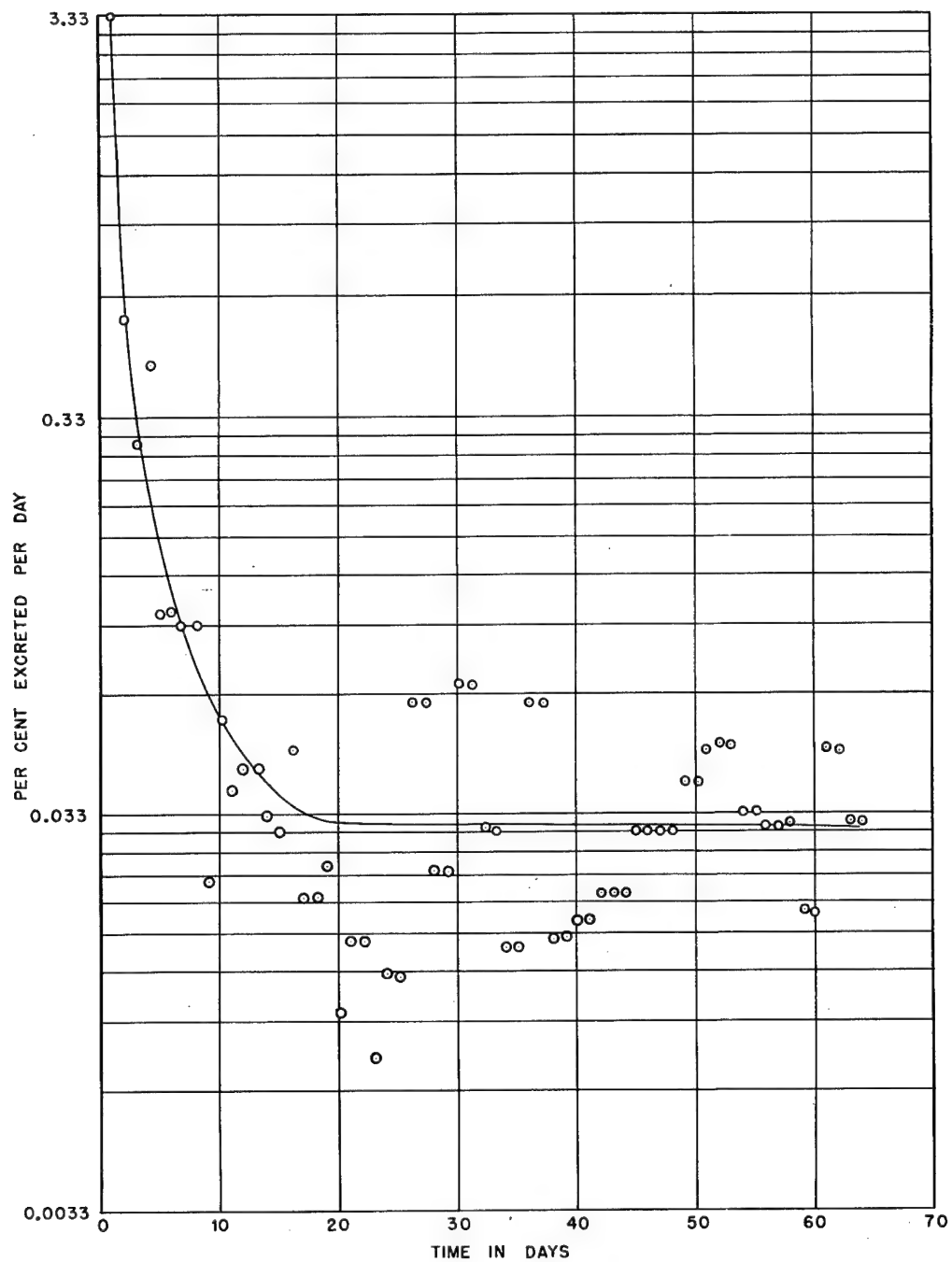
Figure 1. Urinary excretion of fission mixture following intraperitoneal administration.
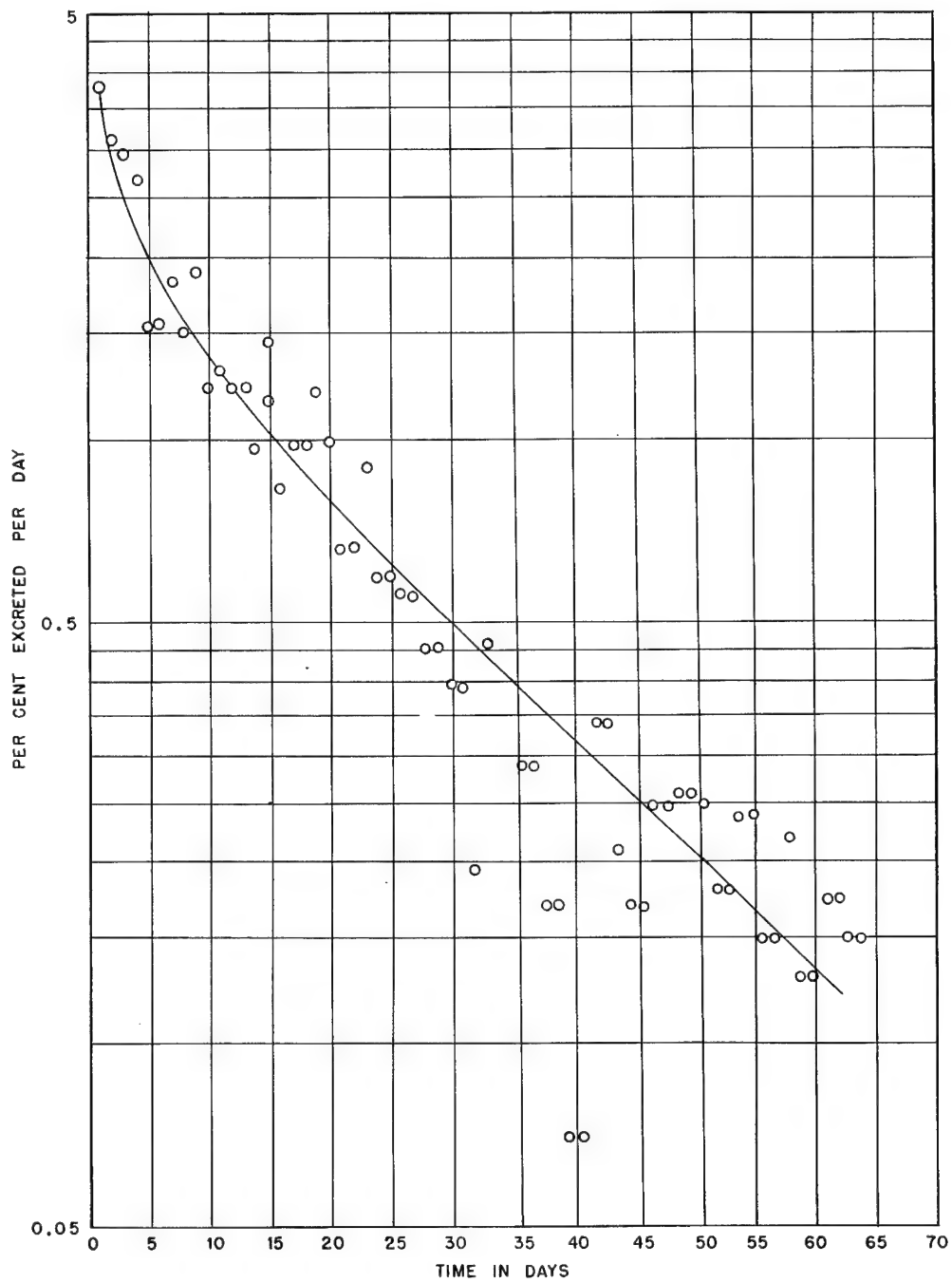
Figure 2. Fecal excretion of fission mixture following intraperitoneal administration.
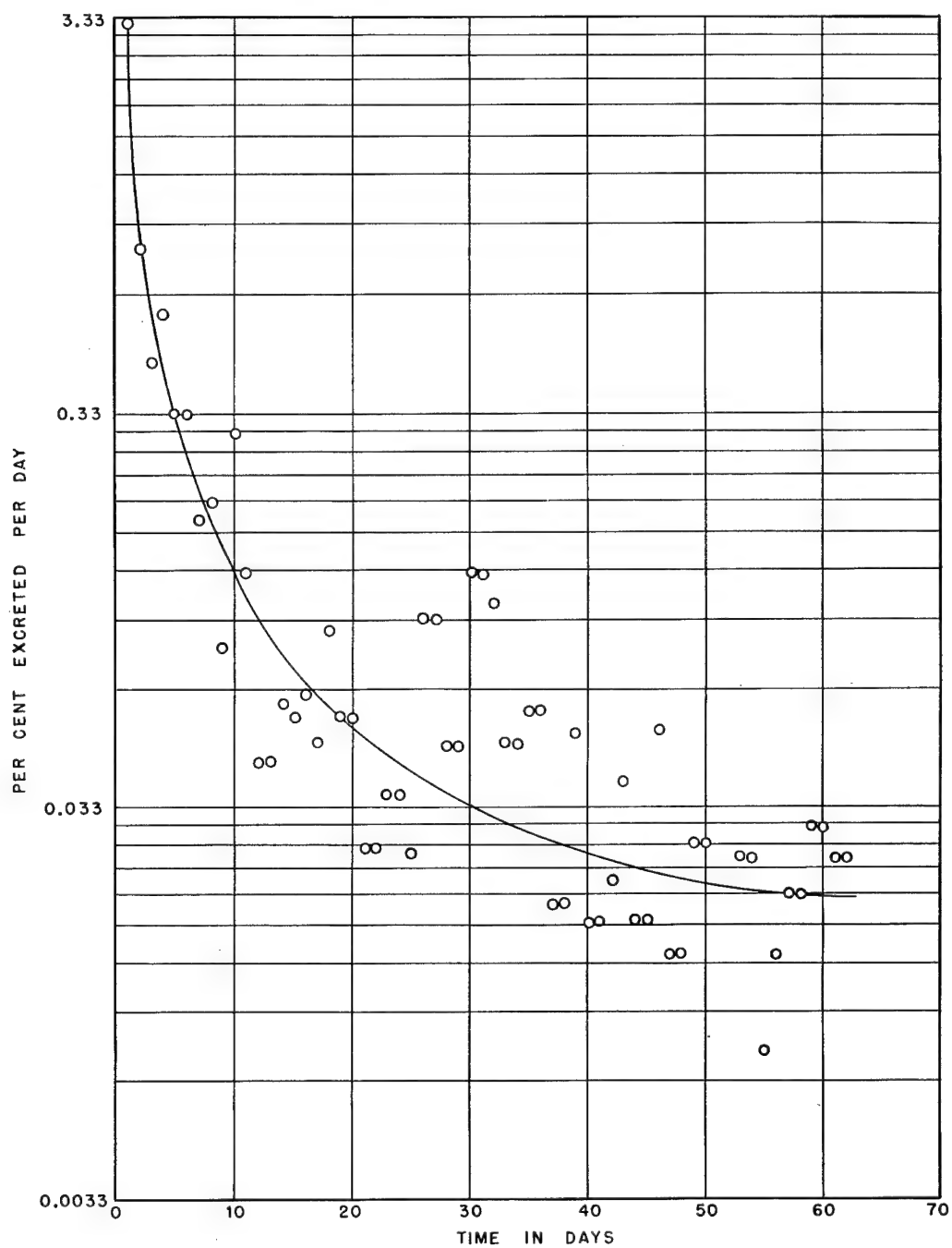
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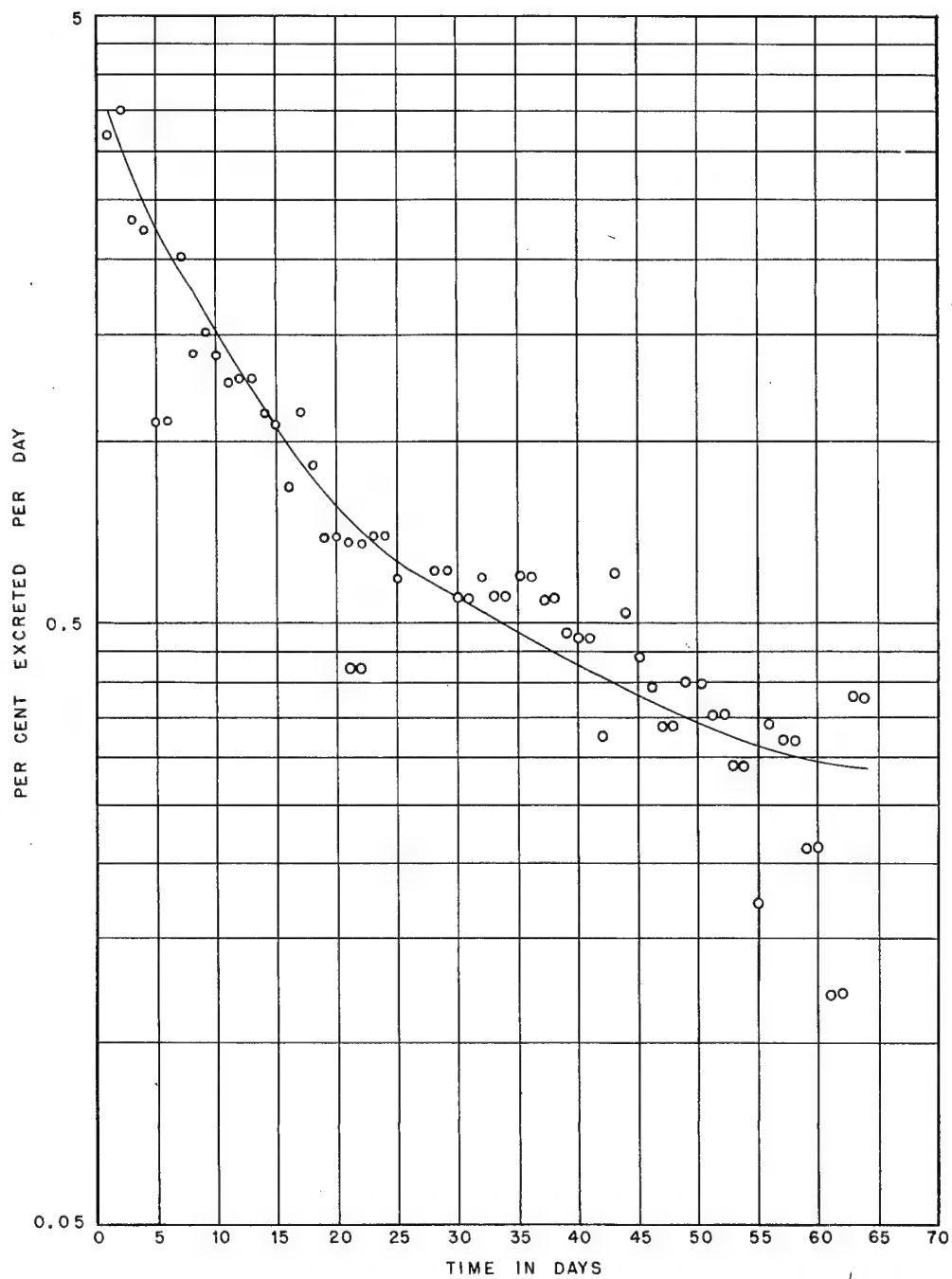Figure 3. Urinary excretion of fission mixture following intramuscular administration.

Figure 4. Fecal excretion of fission mixture following intramuscular administration.

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Table 5

THE DISTRIBUTION OF CARRIER FREE UNSEPARATED FISSION PRODUCTS FOLLOWING ORAL ADMINISTRATION

	FOUR DAYS		SIXTEEN DAYS		SIXTY-FOUR DAYS	
	% UPTAKE PER GRAM	% UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN
Heart	.0021	.0020	.0043	.005	.0038	.004
Liver	.0022	.030	.0023	.017	.001	.010
Kidney	.0027	.0066	.0005	.003	.002	.006
Testes	.0016	.0069	.001	.004		
Spleen	.0045	.0066	.0033	.003	.005	.005
Muscle[1]	.0014	.20	.0018	.27	.0012	.17
Skin[2]	.0016	.068	.0004	.017	.0006	.026
Stomach[3] Sm. Intestines Lg. Intestines	.0124	.230	.0021	.039	.0006	.011
Bone[4]	.1772	3.85	.1372	5.19	.0670	2.08
Lungs	.0028	.0058	.0017	.005	.005	.009
Trachea						
Blood[5]			.0009	.023		
Adrenals						
Lymph Nodes						
Balance[6]	.002	.554	.001	.402	.0003	.103
Total Uptake[7]		4.96		5.69		2.25
Total Urine		5.74		1.50		1.45
Total Feces		89.46		90.60		83.89
Total Recovery		100.16		97.79		87.59

1. Muscle was calculated on basis of 45% of total body weight.
2. Skin was calculated on basis of 42 grams.
3. Gastro-intestinal tract removed and assayed as a unit.
4. Measured value of entire skeleton.
5. Blood was calculated on basis of 8% of total body weight.
6. Balance was measured value for remaining carcass less skeleton & skin, but including blood and muscle.
7. Total uptake value gives fraction present in entire animal at the indicated intervals.
8. Two animals were used in the sixteen day experiment.

The intrapulmonary studies (Table 6) which include radio-autographic studies, concerning which more will be said later, revealed that considerable retention takes place in the lungs, but at sixty-four days the per gram activity in the bone exceeded that of the lungs. The per gram retention in other tissues such as liver, kidney and spleen was much lower than that for either the lungs or bone. This distribution suggests, with respect to radiation damage, the last two tissues mentioned are the ones of primary concern. The relative decrease of retention of activity in the lungs with time suggests that the rate of absorption was greater than the rate of elimination of the absorbed fraction from the rest of the body.

3. Discussion

The rate of elimination at two weeks following intraperitoneal and intramuscular administration was approximately 1% per day, and at four weeks had fallen to a little over .5% per day. With these values in mind it becomes apparent that the rate of excretion of the fission mixture was comparable to the rate of decay of this material after a period of two to three months of cooling. It is difficult to make any more quantitative interpretations due to the fact that a significant proportion of the eliminated material presumably arose from the unabsorbed fraction at the site of injection which was slowly released into the general circulation. From the data presented it is reasonable to assume that the rate of elimination from the skeleton of the material deposited at that point was less than 0.5% per day. On a per gram basis the liver and kidney show a high retention at first but fall much more rapidly than the skeleton.

The high recovery values observed in some of the experiments are presumably the result of the inaccuracy of the self absorption corrections which admittedly are at best only a crude approximation due to the fact that a considerable amount of segregation of the different components of the fission mixture probably took place within the animal.

The percentages indicated for the distribution of activity for the intrapulmonary group are calculated on the distribution of the retained activity within the animal. This method of tabulation is used since no exact procedures for administering a known amount of material and having it all retained within the lung has as yet been worked out. The method employed here, of course, does not take into account the factor of excretion of the absorbed material and thus does not give a direct indication of the elimination throughout the lungs by way of the bronchial tree. The relatively small values for deposition in the trachea would suggest that this latter factor is probably not of too great a significance from the quantitative point of view. It has been found on the average that approximately 1/3rd of the administered dose is either retained by the lungs or deposited elsewhere within the animal tissue. Roughly another 1/3rd is either blown out through the nose or runs out of the mouth at the time of administration and the last 1/3rd is presumably swallowed. The swallowed fraction is, of course, of no significance in those elements which are not absorbed by way of the digestive tract and here is only of minor significance since the maximum amount absorbed by way of the digestive tract is 5% or less. Preliminary experiments with the individual elements from Uranium fission suggests that the bulk of the material held by the lung at the sixty-four day interval was presumably Zirconium, and Columbium and that the bone activity was made up predominately of Strontium, Yttrium, and Cerium with some

Table 6

THE DISTRIBUTION OF CARRIER FREE UNSEPARATED FISSION PRODUCTS FOLLOWING
THE INTRAPULMONARY ADMINISTRATION OF A CHLORIDE SOLUTION

	FOUR DAYS		SIXTEEN DAYS		SIXTY-FOUR DAYS	
	%UPTAKE PER GRAM	% UPTAKE PER ORGAN	%UPTAKE PER GRAM	% UPTAKE PER ORGAN	%UPTAKE PER GRAM	% UPTAKE PER ORGAN
Liver	.36	5.57	.63	7.43	.22	3.49
Kidney	.19	.59	.28	.74	.31	1.00
Spleen	.04	.05	.12	.12	.15	.24
Skin[1]	.01	.46	.04	1.44	.05	2.21
Stomach[2] Sm. Intestine Lg. Intestine	.37	6.76	.05	.93	.08	1.39
Bone[3]	1.99	35.75	3.38	60.73	4.09	73.80
Lungs	18.59	37.91	12.73	21.40	2.90	7.25
Trachea	2.81	.83	.54	.12	.67	.21
Balance[4]	.040	12.27	.028	6.51	.04	11.9

1. Skin calculated on basis of 42 grams
2. Gastro-intestinal tract removed and assayed as a unit.
3. Measured value of entire skeleton.
4. Balance was measured value for remaining carcass less
   skeleton and skin but including blood and muscle.

Barium and Praseodymium during the earlier experiments.

Although these experiments were extended over a period of approximately three months the redistribution of the relative abundance of the principal components in the fission mixture was not great except in the case of Barium. Table 7 lists the relative abundances at the time of isolation and the calculated values at the times when the tissues were measured for the one and four day, sixteen day, and sixty-four day groups.

It is of interest to note that the metabolic picture of the unseparated fission mixture can be approximated by a summation of the metabolic behavior of the individual components.

Table 7

DISTRIBUTION OF ACTIVITIES OF THE FISSION MIXTURE AT THE TIME OF ISOLATION
AND THE VARIOUS INTERVALS WHEN THE TISSUES WERE MEASURED

	Initial Assay	TIME OF MEASUREMENT FOR:		
		One-Four Day	Sixteen Day	Sixty-four Day
Sr	16.1%	17.0	17.2	17.1
Y & Pr	25.0%	25.6	26.3	22.5
Zr	20.4%	20.7	20.7	20.5
Cb	1.63%	1.86	2.00	1.90
Ru	0.24%	0.22	0.21	0.07
Te	0.47%	0.43	0.37	0.02
Cs	0.49%	0.60	0.68	1.44
Ba & La	7.96%	4.50	2.93	.01
Ce	26.5%	27.1	27.6	35.8
$Th(UX_1, UX_2)$	2.42%	1.99	1.71	.50

Part B

RADIO-RUTHENIUM(Ru^{105})

By Roy Overstreet, Louis Jacobson, Harvey Fisher, and Kenneth Scott

1. Preparation Without Carrier

The Ruthenium was isolated from a sample of Uranium metal which had been bombarded with deuterons, (33,000 micro-ampere hours from January 11 to February 13, 1943). The bombarded metal was dissolved in HNO_3 and 1/3rd of the solution was used for the isolation of the Ru^{105}.

Fifty mgs of NaI was added to the dilute HNO_3 solution (3N). The solution was then boiled until all of the Iodine had been expelled.

Ten cc of 60% $HClO_4$ was then added to the Uranium solution. The solution was distilled until fumes of perchloric acid had been evident for five minutes. The distillate was caught in 3N HCl.

The HCl solution of the distillate was made strongly alkaline with NaOH. Cl_2 gas was passed through the solution in a distilling flask until the alkali had been neutralized, as indicated by frothing of the solution. The flask was then heated to boiling for several minutes, the Cl_2 still bubbling through. The distillate was caught in 10cc of concentrated HCl.

The HCl solution of the distillate was evaporated to 0.15cc. The solution was diluted and the pH was adjusted to 2.6 with NaOH. The final volume was adjusted so as to make the solution isotonic in NaCl. The activity of the sample was 241 microcuries on May 14, 1943.

The purity of the Ru^{105} was tested in the following manner: Ten mgs each of Zirconium, Columbium, Tellurium, Lanthanum, Yttrium, Cerium, Thorium, Cesium, Strontium, Barium, Iodine, and Ruthenium were added to a suitable aliquot of the Ru^{105} solution. The Iodine was removed by distillation with dilute HNO_3 and found to be inactive. The Ruthenium was removed from the Iodine-free solution by distillation with perchloric acid. The residue was then examined for activity. It was found that the Ruthenium was at least 37.6% pure. An absorption curve was made and is shown in Figure 5.
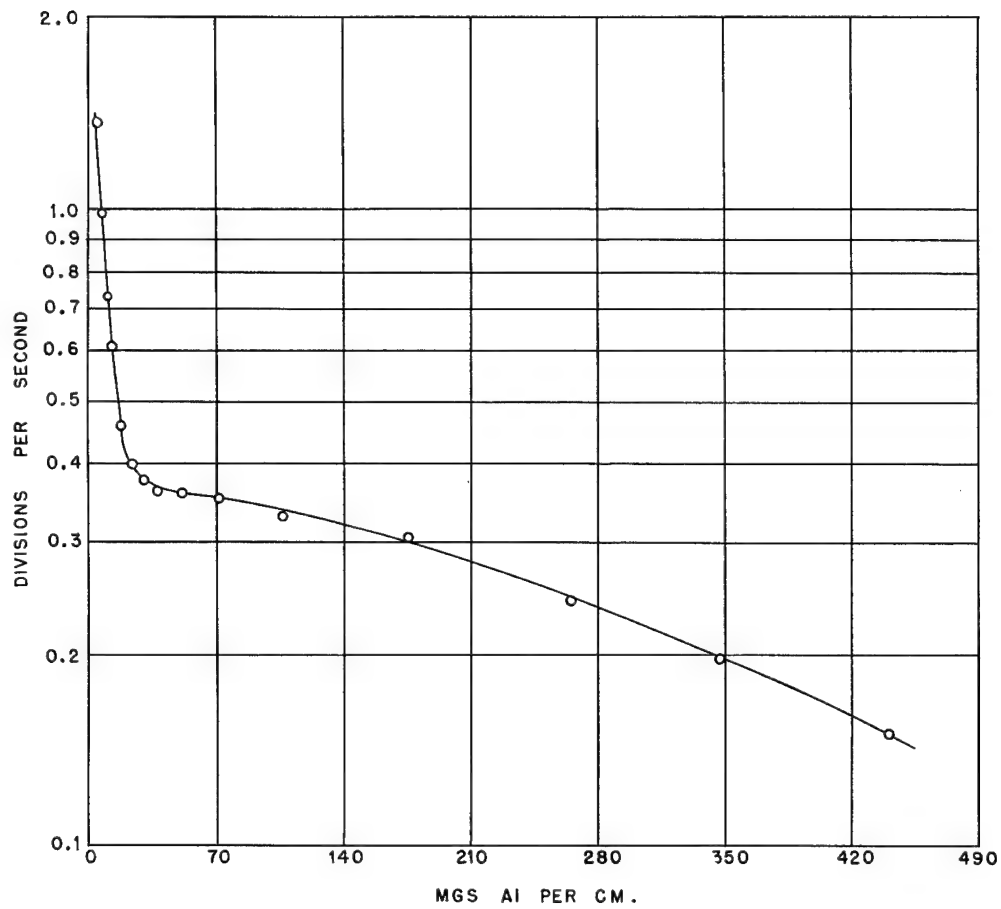
Figure 5. Al absorption curve for Ruthenium (Ru$^{<105}$).

2. Tracer Studies

Method.

A purified preparation of carrier free Ru^{105} in an isotonic solution of Sodium Chloride at pH 2.6 was injected into the following groups of three animals each: Four intraperitoneal, three intramuscular, four intrapulmonary, and one oral. The intraperitoneal animals were sacrificed at one, four, sixteen, and sixty-four days. The intramuscular groups at four, sixteen and sixty-four days, the intrapulmonary animals at four, sixteen, thirty-two and sixty-four days, and the oral group at four days. Tissues and excreta were collected as in the previous experiments. Considerable difficulty was encountered in the ashing of Ruthenium containing tissue due to the loss occurred but that no volatilization took place at temperatures ranging from 250°C to 300°C. All tissue samples such as liver, heart, bone, etc. were ashed at this lower level in small metal capsules. The excreta, carcass, skeleton, skin and Gastro-Intestinal tract were dissolved in 15% Sodium Hydroxide at 100°C. This treatment of the carcass made it possible to separate the bones from the residue of the carcass. The solutions were brought to a standard value and aliquot samples measured for radioactive assay.

The skeleton was dried, ground, and a weighed portion measured for its Ru^{105} content. It was found that some of the Ru^{105} was leached from the skeleton by the alkali digestion for which a correction had to be made. This correction factor was determined by a comparison of the Ru^{105} content of an unleached bone sample with a comparable leached specimen. For these determined values it was then possible to correct for the leaching factor by subtracting a portion of the measured activity from the balance and adding it to the skeleton. Corrections for the mass absorption factor were made by adding measured amounts of water to a series of small dishes containing a known amount of $RuCl_4$. This method has been found to be more accurate and satisfactory than the previous procedure which involved the use of solutions of known amounts of Sodium Chloride that were subsequently evaporated to dryness.

3. Discussion

Results:

The distribution of Ru^{105} without carrier in the tissue following both intraperitoneal and intramuscular injection (Tables 8-10) revealed that this element was not selectively deposited in the skeleton as compared to other tissues but instead was distributed more evenly throughout all tissues than most elements studied thus far. The two striking exceptions to this generalization were the relatively high values noted in the kidney and the very low uptake in the brain. In the intramuscular group it is of interest to note that at the end of four days almost 3/4ths of the injected dose had been absorbed but thereafter no very significant further increase in absorption took place. The factor of contamination of abdominal organs was very striking in the intraperitoneal group. Aside from this there were no very significant differences between the two routes of administration.

Table 8

THE DISTRIBUTION OF CARRIER FREE RADIO-RUTHENIUM FOLLOWING
INTRAPERITONEAL INJECTION

	ONE DAY[8]		FOUR DAYS	
	% UPTAKE PER GRAM	% UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN
Heart	.14	.14	.16	.17
Liver	1.19	17.95	.47	5.76
Kidney	.704	2.28	1.16	2.99
Testes	.15	.58	.23	.83
Spleen	.63	.90	.70	1.15
Muscle[1]	.048	6.20	.062	7.87
Skin[2]	.12	5.70	.15	7.27
Stomach	.48	1.69	.20	.69
Sm. Intestine	.44	6.10	.24	2.16
Lg. Intestine	.24	.10	.38	.22
Bone[3]	.13	4.93	.33	6.63
Brain	.012	.014	.009	.14
Lungs	.41	.86	.30	.70
Belly Muscle[4]	.85		.41	
Fat			.22	
Blood[5]	.34	7.94	.26	5.80
Adrenals	.098	.008	.25	.022
Lymph Glands	.005		.13	
Feces[6]			.077	
Balance[7]		27.96		18.65
Total Urine		13.20		34.91
Total Feces		11.10		13.32
Recovery		93.51		95.61

1. Muscle was calculated on basis of 45% of total body weight.
2. Animals skinned. Measured value for entire skin.
3. Measured value for entire skeleton.
4. A sample of muscle from the anterior abdominal wall at the site of injection.
5. Blood was calculated on basis of 8% of total body weight.
6. Sample of feces removed from large intestines when animals were sacrificed.
7. Balance was measured value of remaining carcass less skeleton and skin, but including blood and muscle.
8. Two animals were used in the one day experiment.

Table 9

THE DISTRIBUTION OF CARRIER FREE RADIO-RUTHENIUM FOLLOWING
INTRAPERITONEAL INJECTION (CONTINUED)

	SIXTEEN DAYS		SIXTY-FOUR DAYS	
	% UPTAKE PER GRAM	% UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN
Heart	.054	.049	.030	.031
Liver	.19	1.94	.057	.98
Kidney	.71	1.57	.17	.45
Testes	.17	.56	.087	.32
Spleen	.34	.43	.17	.20
Muscle[1]	.029	3.22	.012	2.01
Skin[2]	.10	4.50	.049	3.41
Stomach	.086	.30	.037	.13
Sm. Intestine	.18	1.58	.059	1.84
Lg. Intestine	.13	.073	.056	.026
Bone[3]	.16	5.97	.056	2.93
Brain	.002	.005	<.001	<.001
Lungs	.11	.16	.048	.098
Belly Muscle[4]	.32		.081	
Fat	.054		.025	
Blood[5]	.014	.28	<.001	.03
Adrenals	.18	.01	.12	.005
Lymph Glands	.077		.02	
Feces[6]	.012		.057	
Balance[7]		6.97		5.94
Total Urine		35.66		45.27
Total Feces		39.49		47.17
Recovery		99.26		108.80

1. Muscle was calculated on basis of 45% of total body weight.
2. Animals skinned. Measured value for entire skin.
3. Measured value for entire skeleton.
4. A sample of muscle from the anterior abdominal wall at the site of injection.
5. Blood was calculated on basis of 8% of total body weight.
6. Sample of feces removed from large intestines when animals were sacrificed.
7. Balance was measured value of remaining carcass less skeleton and skin, but including blood and muscle.

Table 10

THE DISTRIBUTION OF CARRIER FREE RADIO-RUTHENIUM FOLLOWING INTRAMUSCULAR INJECTION

	FOUR DAYS		SIXTEEN DAYS		SIXTY-FOUR DAYS [8]	
	% UPTAKE PER GRAM	% UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN
Heart	.080	.076	.040	.039	.023	.028
Liver	.17	2.07	.11	1.08	.014	.23
Kidney	.97	2.50	.58	1.23	.13	.42
Testes	.088	.32	.091	.30	.027	.10
Spleen	.26	.32	.26	.29	.044	.061
Muscle[1]	.046	5.33	.028	3.29	.016	3.07
Skin[2]	.11	4.88	.086	3.47	.072	3.03
Stomach	.031	.11	.023	.081	.014	.048
Sm. Intestines	.064	.77	.052	.44	.0053	.16
Lg. Intestines	.076	.043	.058	.051	.020	.008
Bone[3]	.21	7.34	.14	4.66	.046	3.19
Brain	.003	.005	.001	.001	<.001	<.001
Lungs	.14	.25	.077	.13	.033	.070
Belly Muscle Unab. in left leg.[4]		27.0		18.10		23.35
Fat	.057		.053		.009	
Blood[5]	.096	1.99	.009	.20	<.001	.04
Adrenals	.22	.01	.11	.005		
Lymph Glands	.071		.03			
Feces[6]	.019		.015		<.001	
Balance[7]		5.76		5.76		1.41
Total Urine		38.93		45.86		53.05
Total Feces		7.79		24.39		28.57
Recovery		98.17		105.99		113.72

1. Muscle was calculated on basis of 45% of total body weight.
2. Animals skinned. Measured value for entire skin.
3. Measured value for entire skeleton.
4. Unabsorbed fraction in left leg.
5. Blood was calculated on basis of 8% of total body weight.
6. Sample of feces removed from large intestines when animals were sacrificed.
7. Balance was measured value of remaining carcass less skeleton and skin but including blood and muscle.
8. Two animals were used in the sixty-four day experiment.

The elimination studies with $Ru^{>105}$ without carrier revealed that on the average approximately 30% was eliminated in the first 24 hours by way of the urine (Figures 6-9). Thereafter the rate fell rapidly and at the end of four weeks was approximately 0.15% per day and remained at that level throughout the remainder of the experiments. The rate of fecal elimination was slower during the first two or three days but by the end of the second day became greater than the rate of urinary excretion. The total elimination over the sixty-four day period in the intraperitoneal and intramuscular groups indicated that over 80% of the administered dose was excreted during this interval after corrections for recovery and the unabsorbed Ruthenium had been made.

From a practical standpoint the rate of elimination of Ruthenium is such that it is significantly greater than the rate of radioactive decay of the 30-day Ruthenium and far greater than that of the 300-day Ruthenium.

No significant absorption of Ruthenium took place from the digestive tract.

The intrapulmonary experiments showed (Table 11) a high degree of retention by the lungs. The values given represent the distribution of $Ru^{>105}$ in terms of retained activity in the animals. The rate of excretion was indirectly determined by comparing the average total $Ru^{>105}$ content of the animals for the different groups. These values showed approximately the same relative changes with time as did the corresponding retention values for the intraperitoneal and intramuscular groups. This observation together with the relatively low activity values for the trachea and the radio-autographic findings indicate that the elimination of $Ru^{>105}$ by the lungs occurs chiefly by way of absorption.
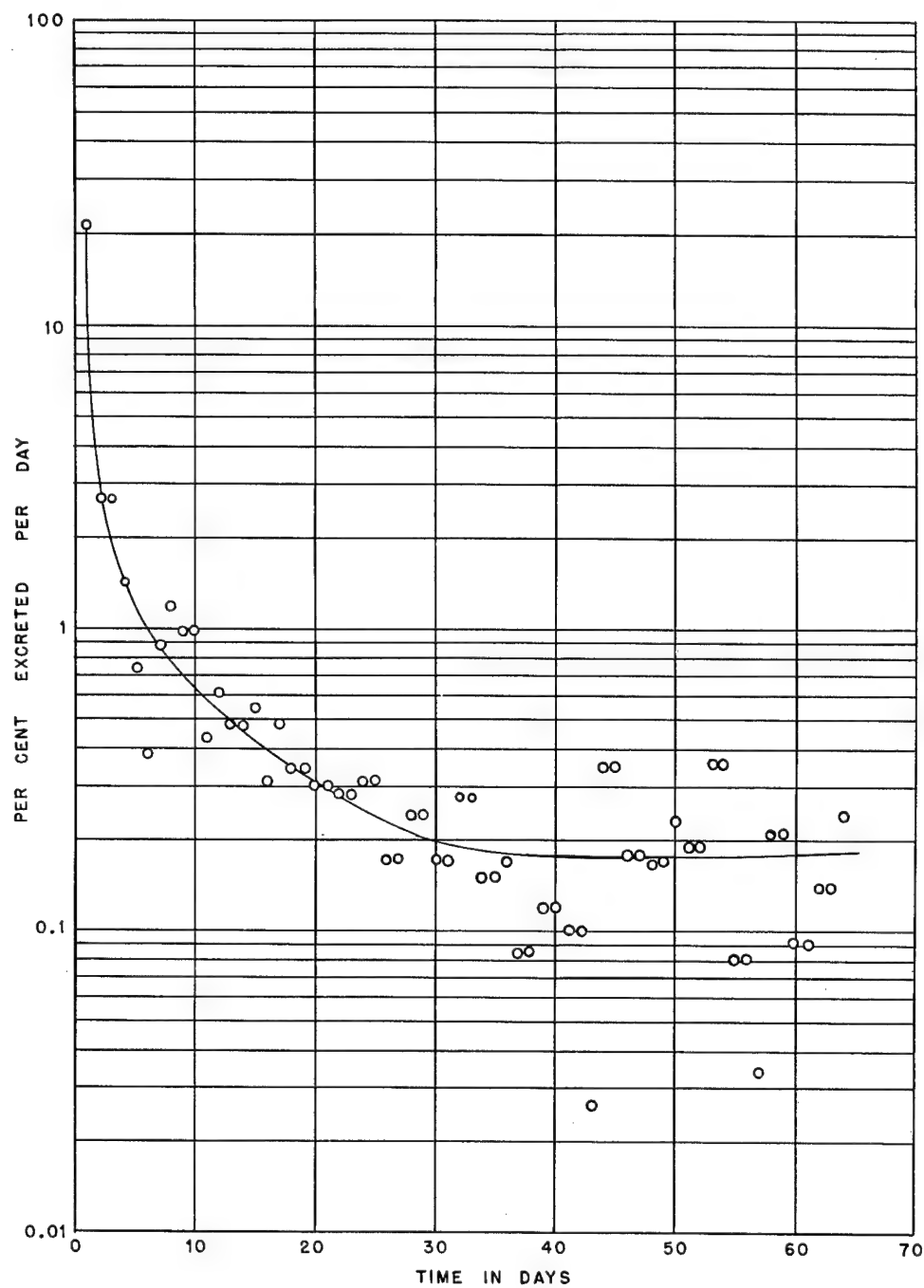
Figure 6. Urinary excretion of Ru $^{>105}$ without carrier following intraperitoneal administration.
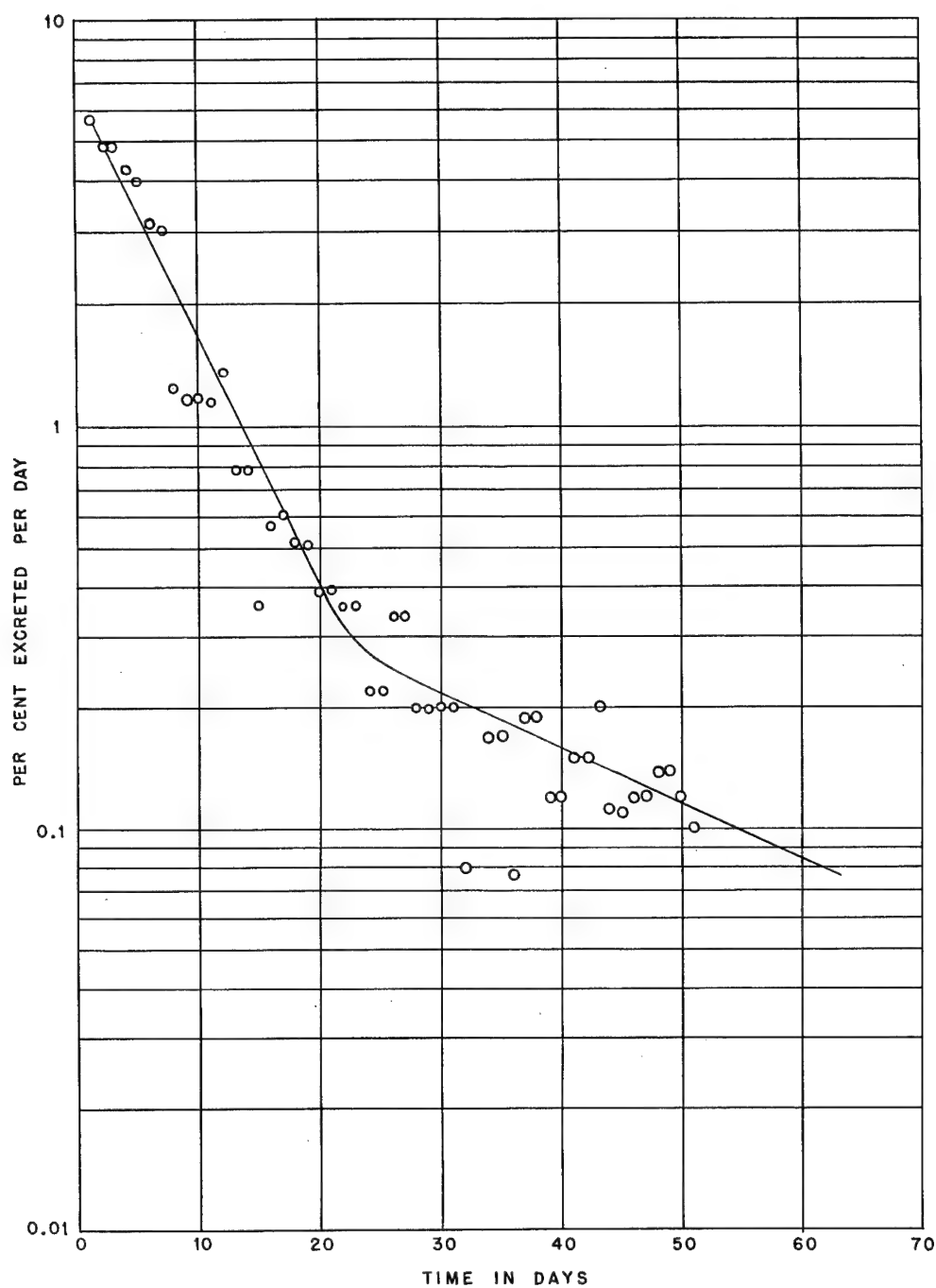
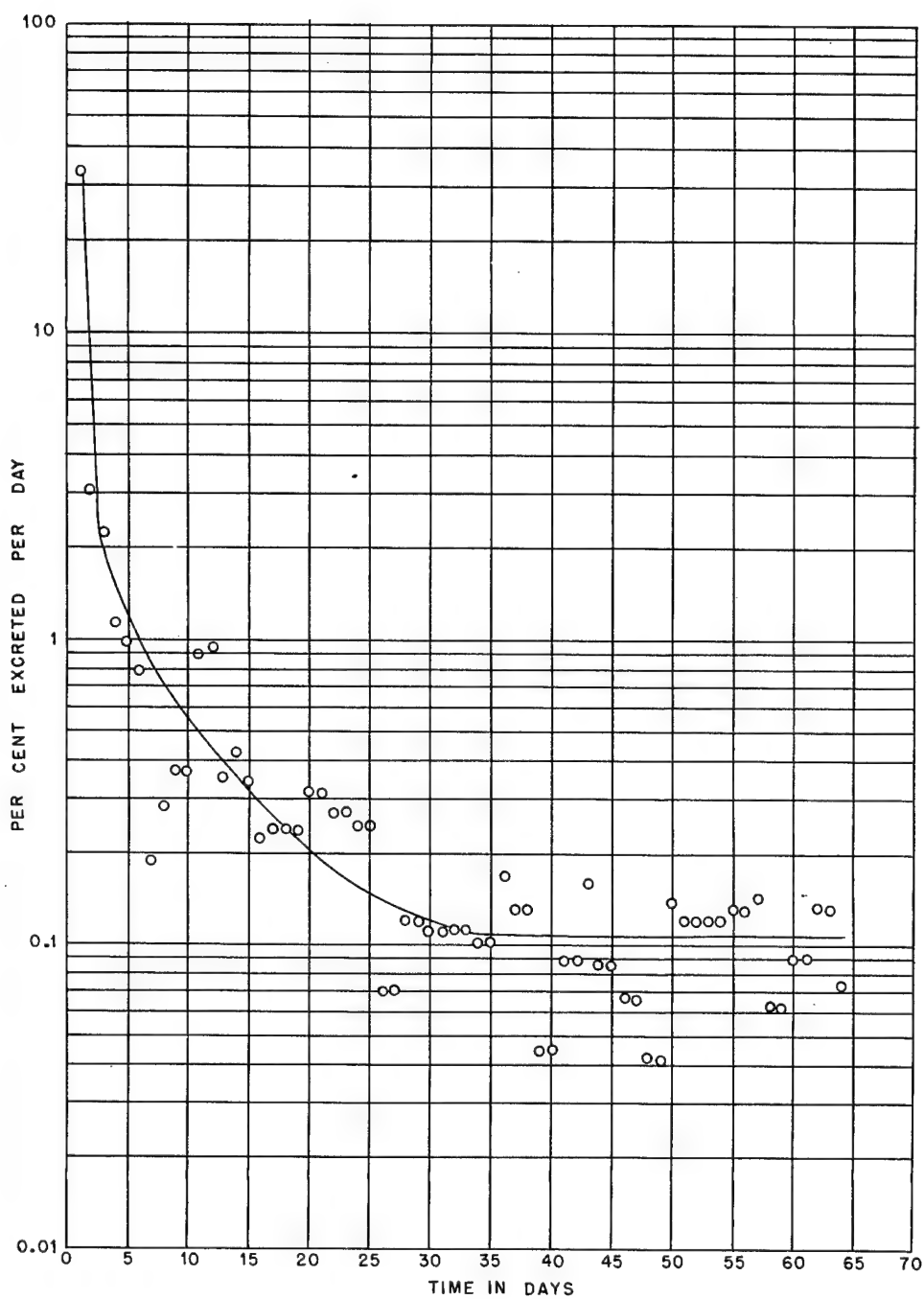Figure 7. Fecal excretion of Ru $^{>103}$ without carrier following intraperitoneal administration.

Figure 8. Urinary excretion of Ru$^{>105}$ without carrier following intramuscular administration.
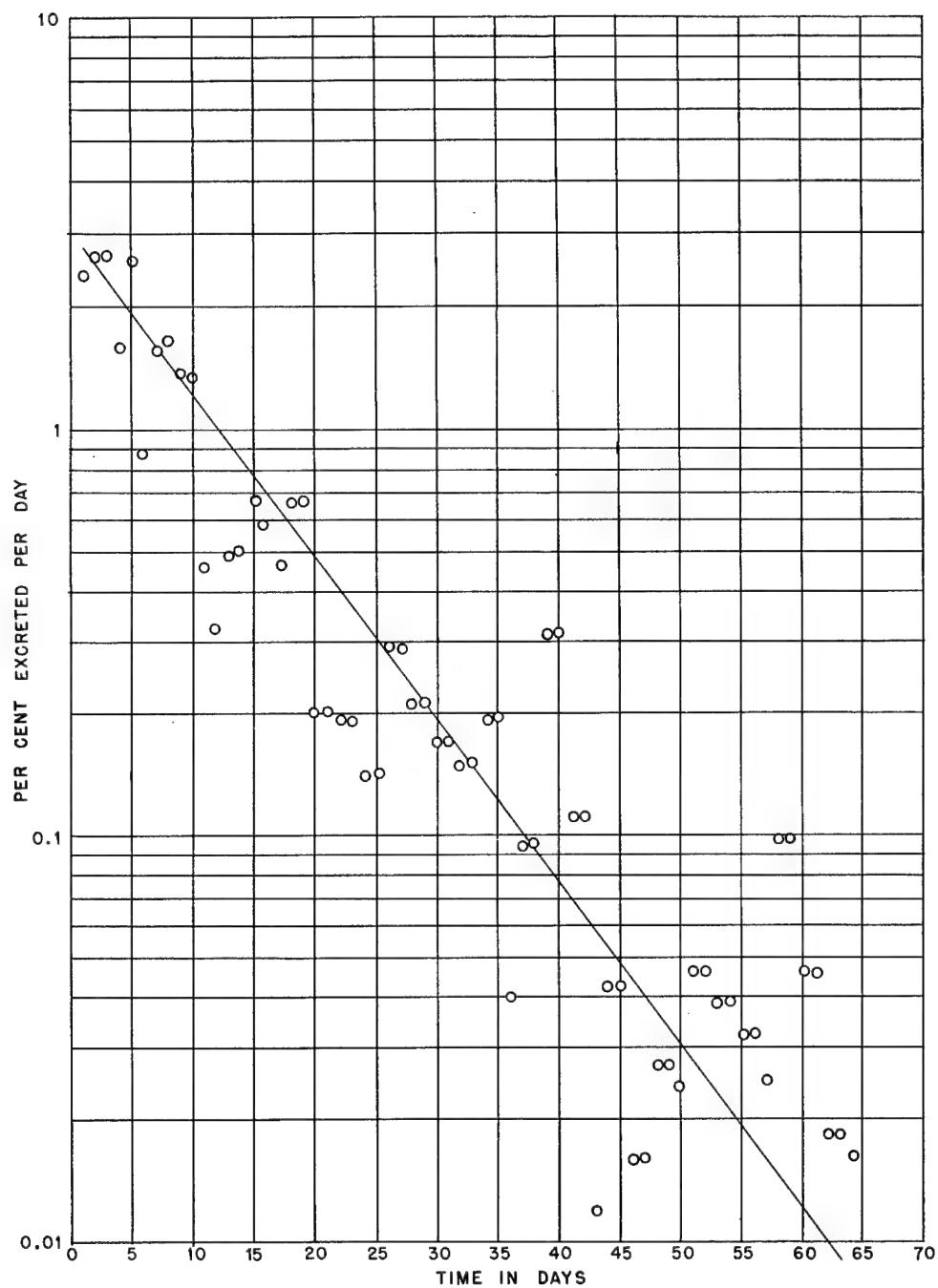
Figure 9. Fecal excretion of Ru$^{>105}$ without carrier following intramuscular administration.

Table 11

THE DISTRIBUTION OF CARRIER FREE RADIO-RUTHENIUM FOLLOWING INTRAPULMONARY ADMINISTRATION

	FOUR DAYS		SIXTEEN DAYS	
	% UPTAKE PER GRAM	% UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN
Heart			.12	.15
Liver	.20	3.20	.22	2.95
Kidney	1.36	4.73	2.38	7.59
Testes			.14	1.14
Spleen	.47	.70	.42	.75
Muscle[1]			.06	8.86
Skin[2]	.18	7.57	.01	.48
Gastro-Intes. Tract[3]	.24	4.44	.02	.37
Bone[4]	.13	2.45	.37	7.42
Lungs	23.6	63.6	20.8	58.4
Trachea	.43	.17	.32	.14
Balance[5]	.07	13.6	.07	14.9

	THIRTY-TWO DAYS		SIXTY-FOUR DAYS	
Heart	.27	.46	.16	.23
Liver	.25	3.17	.17	2.65
Kidney	1.37	4.01	1.41	4.47
Testes			.20	.93
Spleen	.45	.54	.34	.43
Muscle[1]	.09	12.2	.09	12.9
Skin[2]	.42	17.5	.37	15.4
Gastro-Intes. Tract[3]	.24	4.72	.15	2.98
Bone[4]	.35	7.29	.30	7.34
Lungs	21.0	50.3	12.6	25.5
Trachea	.3	.12	.5	.21
Balance[5]	.06	11.0	.19	38.3

1. Muscle was calculated on basis of 45% of total body weight.
2. Animals skinned, measured value for entire skin.
3. Gastro-Intestinal tract removed and assayed as a unit.
4. Measured value for entire skeleton.
5. Balance was measured value of carcass less skeleton and skin but including blood and muscle.

Part C

NEPTUNIUM (Np^{238}, Np^{239})

By Roy Overstreet, Louis Jacobson, Harvey Fisher, and Kenneth Scott

1. Preparation

A plate of Uranium was bombarded with 93.8 micro-ampere hours of 16Mev deuterons.

Twenty-four hours later the surface of the plate was treated repeatedly with a mixture of concentrated HNO_3 and concentrated HCl. By this treatment about 80% of the activity was dissolved off the target. The solution was converted to the Nitrate by repeated evaporations with HNO_3. The residue was dissolved in 140cc of water.

The Uranium solution was acidified with 7 cc of concentrated H_2SO_4 and 20mgs of Lanthanum was added. The solution was made 2N in HF and the LaF_3 was centrifuged out and washed with 1N HF.

The LaF_3 precipitate was treated with 1cc of 10N H_2SO_4 and evaporated to fuming. The mixture was diluted to 5cc and treated with 100 mgs $K_2S_2O_8$ and 0.75 mgs of Ag+. The material was heated on the steam bath for thirty minutes. The mixture then cooled and 100 mgs more of $K_2S_2O_8$ was added. After standing for thirty minutes, the mixture was made 2N in HF and centrifuged. The precipitate was washed with 1N HF and the supernatant liquid and washings were combined.

The combined supernatant liquid and washings were evaporated to fuming of H_2SO_4, diluted with 3 drops of water, and treated with SO_2 gas. The mixture was again evaporated to fuming and then diluted to 5cc, 4mgs of Lanthanum was added and the solution was made 2N in HF. The resulting LaF_3 precipitate was centrifuged out and washed with 1N HF.

The LaF_3 precipitate was fumed with 0.1cc of concentrated H_2SO_4 and then diluted to 2cc. Fifteen mgs of $K_2S_2O_8$ and 0.2 mgs of Ag+ were added. The solution was heated on the steam bath for 1/2 hour and then cooled. Fifteen mgs of $K_2S_2O_8$ and the solution was made 2N in HF. The LaF_3 was centrifuged out and washed with 1N HF. The supernatant liquid and washings were combined.

The combined supernatant liquid and washing was evaporated to fuming, diluted with 3 drops of water, treated with SO_2, and again heated to fuming, and material dissolved in 3cc of water. 0.2mgs of Fe was added and the solution was made basic with carbonate free NH_4OH. The $Fe(OH)_3$ was centrifuged out and washed with 0.1N NH_4OH.

The $Fe(OH)_2$ was dissolved in .05cc of concentrated HCl. The solution was diluted and the pH was adjusted to 2.6 with dilute NaOH. The volume was finally made up to 15.0cc, and was isotonic in NaCl. The decay and absorption curves are shown in Figures 10 and 11.
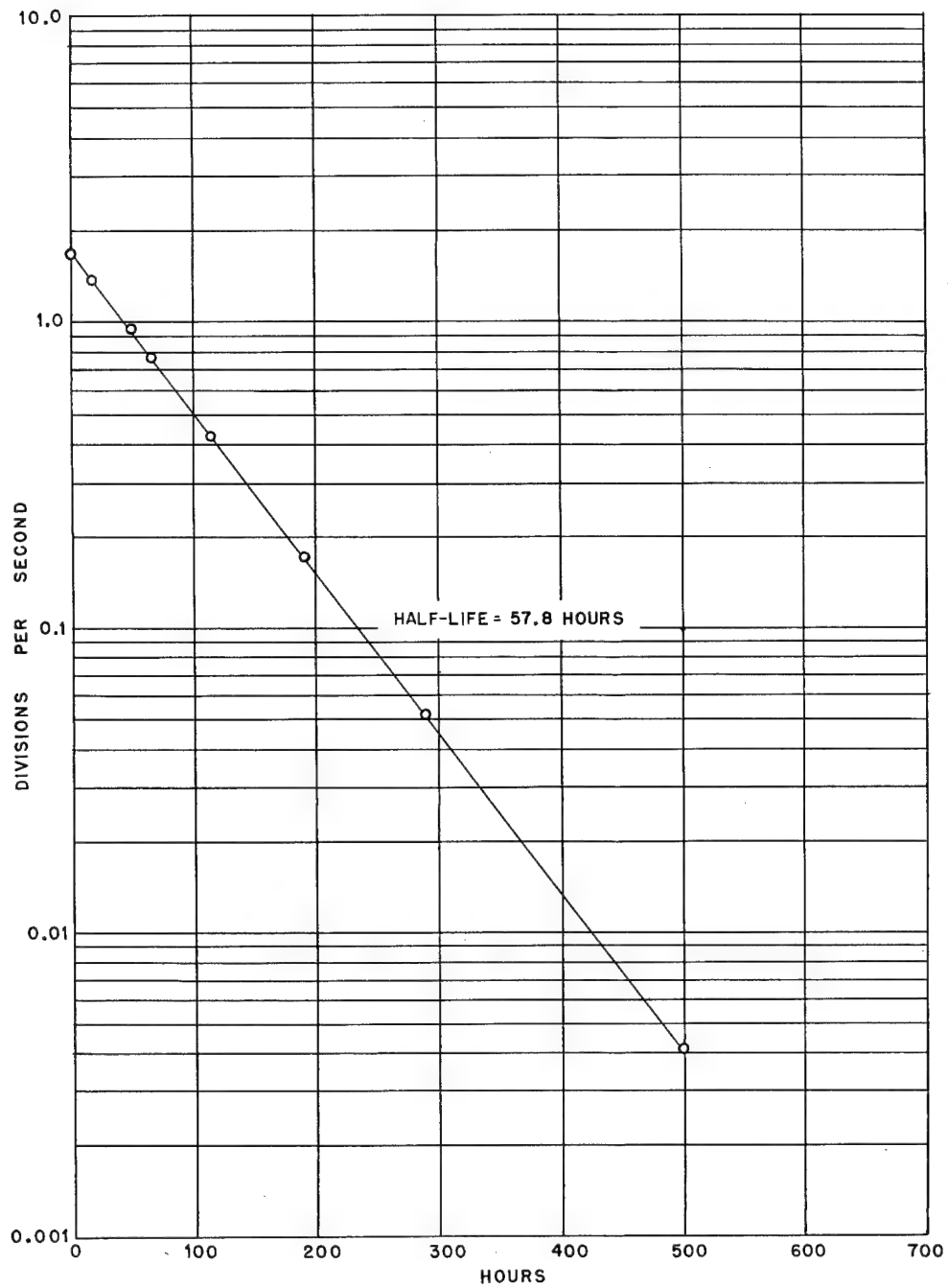
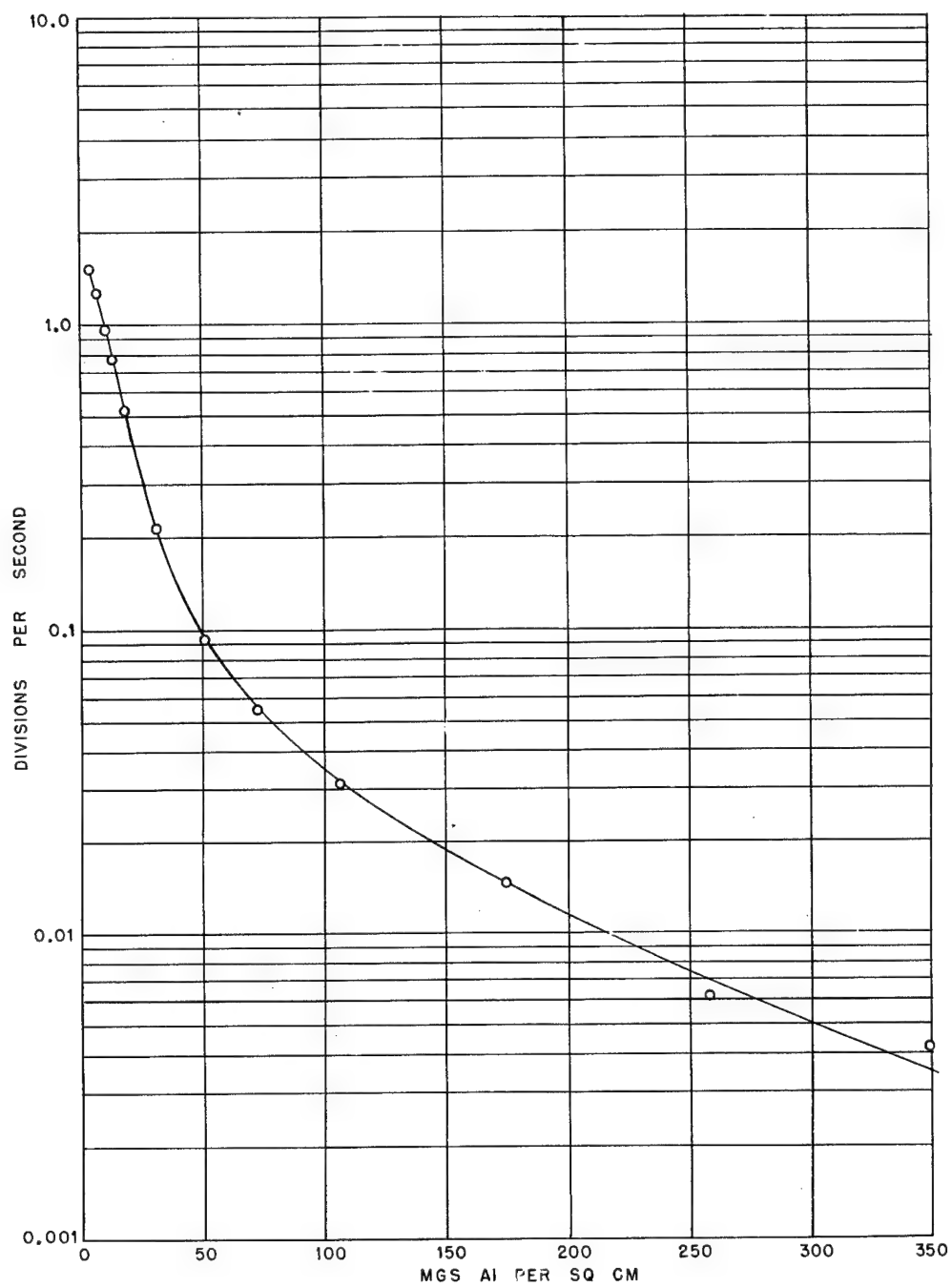Figure 10. Decay curve for Neptunium (Np^{238}, Np^{239}).

Figure 11. Al-absorption curve for Neptunium (Np[238], Np[239]).

It might be kept in mind that Np^{238} was present in the sample which slightly modified both curves.

2. Tracer Studies

Method: An isotonic NaCl solution at pH 2.6 containing $Np^{238,239}$ free from radioactive contaminants and inert hold-back carrier was administered to the following groups of three rats each: Three intramuscular, three intrapulmonary, and one oral . The intramuscular and intrapulmonary groups were sacrificed at one, four, and eight days and the oral group at four days. The excreta of the intramuscular and oral groups was collected at daily intervals. The tissues were removed, ashed at 300°C and measured as in other tracer studies. A series of measurements were made at varying ashing temperatures to check against possible loss by volatilization. Suitable mass absorption curves were prepared for applying the necessary corrections to the measured tissue samples.

Results: Table 12 shows the distribution pattern of Neptunium following intramuscular injection. The skeleton was the chief point of deposition. Kidney and Liver showed the next highest concentration of Neptunium per gram unit weight .

The pulmonary studies (Table 13) showed that the pulmonary retention was considerably less than for the other rare earths, Zirconium, Columbium, and Ruthenium. The absorbed fraction was deposited primarily in the skeleton. Considerable retention also occurred in the kidneys and liver. The oral absorption was less than 0.1%. Elimination (Table 13) was relatively rapid and during the first few days more was excreted by the kidneys.

3. Discussion

The metabolic behavior of Neptunium in the reduced state resembles that of Yttrium more than any of the other rare earths. If the possibility of accidental ingestion of Np^{237} exists it might be desirable to do some long term experiments with this isotope of Neptunium since the short half-lives of Np^{238} and Np^{239} prevent a period of study longer than the 8 day intervals reported here.

Although the degree of pulmonary retention is considerably lower for Neptunium than for Yttrium, Zirconium, Columbium, Ruthenium, Lanthanum, Cerium, and Praseodymium the activity per gram of lung is still considerably higher than for bone.

Table 12

THE DISTRIBUTION OF NEPTUNIUM FOLLOWING INTRAMUSCULAR ADMINISTRATION

	ONE DAY		FOUR DAYS		EIGHT DAYS	
	% UPTAKE PER GRAM	% UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN	% UPTAKE PER GRAM	% UPTAKE PER ORGAN
Heart	.007	.007	.009	.007	.018	.016
Liver	.30	3.58	.31	2.81	.28	2.47
Kidney	.74	1.73	.37	.83	.31	.72
Testes	.006	.019	.010	.035	.006	.021
Spleen	.030	.027	.049	.067	.035	.022
Muscle[1]	.003	.36	.003	.38	.002	.28
Skin[2]	.010	.42	.006	.23	.006	.26
Stomach	.009	.017	.006	.010	.007	.015
Sm. Intestine	.015	.17	.009	.076	.011	.10
Lg. Intestine	.024	.017	.010	.007	<.005	<.003
Bone[3]	1.58	40.68	1.76	36.30	1.89	42.69
Brain	<.0005	<.001	.007	.011	<.002	<.003
Lungs	.028	.046	.021	.033	.028	.053
Fat	.003		.005		.007	
Blood[4]	.009	.20	.004	.071	.019	.41
Adrenals	<.01	.0005	.05	.002	.022	.001
Lymph Nodes	.007		.025		.035	
Feces[5]	.32		.058			
Leg[6]		45.70		42.27		26.38
Balance[7]		7.17		4.75		3.41
Urine		8.65		17.85		11.87
Feces		9.70		10.34		25.43
Recovery		117.50		113.40		113.21

1. Muscle was calculated on basis of 45% of total body weight.
2. Skin calculated on basis of 42 grams.
3. Measured value for entire skeleton.
4. Blood was calculated on basis of 8% of total body weight.
5. Sample of feces removed from large intestines when animals were sacrificed.
6. Unabsorbed fraction in left leg.
7. Balance was measured value for the remaining carcass less the skeleton, but including skin, blood, and muscle.

Table 13

THE DISTRIBUTION OF NEPTUNIUM FOLLOWING INTRAPULMONARY ADMINISTRATION

	ONE DAY		FOUR DAYS		EIGHT DAYS	
	%UPTAKE PER GRAM	%UPTAKE PER ORGAN	%UPTAKE PER GRAM	%UPTAKE PER ORGAN	%UPTAKE PER GRAM	%UPTAKE PER ORGAN
Heart	.01	.02				
Liver	.55	6.52	.43	4.52	.22	3.17
Kidney	1.17	3.48	.70	1.52	.24	.61
Testes	.02	.05				
Spleen	.04	.05			<.05	<.05
Muscle	.005		<.01		<.01	
Skin[1]			.06	3.54	.05	2.56
Stomach [2] Sm. Intestine Lg. Intestine			.46	5.81	.09	1.57
Bone[3]	3.34	56.30	4.30	63.60	2.68	67.00
Lungs	9.07	18.57	7.78	13.40	5.74	9.75
Trachea	1.25	3	.01			
Balance[4]		14.34		7.12		15.60

1. Animals skinned, measured value for entire skin.
2. Gastro-Intestinal tract removed and assayed as a unit.
3. Measured value for entire skeleton.
4. Balance was measured value of remaining carcass less skeleton and skin, but including blood and muscle.

THE EXCRETION OF NEPTUNIUM FOLLOWING INTRAMUSCULAR INJECTION

DAYS	URINE AVERAGE	FECES AVERAGE
1	7.25	6.62
2	6.55	5.08
3	.90	1.01
4	.35	2.65
5	.11	1.33
6	.23	.99
7	.23	.99
8	.19	4.90
TOTAL	15.61	23.57

Part D

RADIO-AUTOGRAPHIC STUDIES

By Dorothy Axelrod

1. Unseparated Fission Products Without Carrier

General Method:

One lung was removed from each group of the intrapulmonary animals and fixed in formalin (in later experiments Zenker-formol was used) in order to obtain better histological sections. Paraffin sections of 8-10 micron thickness were cut. The sections were mounted on glass slides, the paraffin washed off with xylene, and the slides then dipped in celloidin and allowed to dry. This procedure serves to remove the paraffin and to provide the sections with a protective covering for the subsequent exposure.

The prepared sections were placed in contact with Agfa No-Screen X-ray Film, wrapped with light-proof black paper, and placed under lead blocks to keep the film in close contact with the sections. An adequate exposure requires that from 2,000,000 to 10,000,000 beta particles must strike each square centimeter of the film emulsion. The time required for such an exposure is, of course, dependent upon the number of radioactive atoms in the sample and their half-life. In practice it has been found for these studies that exposure periods range from one to sixty days.

Following the exposure, the film is developed and a new film mounted on the section if the first exposure was either too light or too heavy. It is desirable to prepare a heavy and light exposure from each section so that a maximum of detail may be obtained.

After a number of satisfactory radio-autographs have been prepared the sections are stained. Each section and its corresponding radio-autographs are carefully examined under a microscope. The regions of greatest blackening represent areas of accumulation of the radioactive material in the tissue section. Typical examples of the radio-autographic pattern are selected and photo-micrographs of the sections and their corresponding radio-autographs are prepared.

The resolution obtainable by this technique is from 25 to 50 microns due to the scattering of the beta particles in the emulsion and the glass plate upon which the sections are mounted.

Care must be taken so that no leaching effect takes place from the various histological techniques to which the tissues are subjected. For example, the presence of formic acid in the formaldehyde would probably leach out from the tissue substances such as the rare earths and thus distort the radio-autographic patterns. In each series of experiments

precautions are taken against such probable factors and in addition a careful check on the fixing fluids, dehydrating agents, etc. for the presence of radioactivity is made. Thus far no difficulty in this direction has been encountered. The experiments include studies with Yttrium, Zirconium, Columbium, Ruthenium, Cerium, Praseodymium, Neptunium, and unseparated fission products.

Fission Mixture Results

Photo-micrographs of lung sections and their corresponding radio-autographs from the four, sixteen, thirty-two and sixty-four day intrapulmonary experiments are shown in Figures 12-16. It can be clearly seen that the activity was distributed in a patchy manner throughout the parenchyma of the lung and was absent from the blood vessels, bronchi, and lymphoid tissue. There was a definite tendency of the darkened areas in four, and sixteen day experiments to follow the pattern of the alveolar structure of the lung. This effect was not present at the thirty-two and sixty-four day period.

Discussion:

The presence of apparently excessive amounts of lymphoid-appearing tissue around the larger bronchi was probably due to pulmonary infection. The rats used were carefully selected, but at the time of these studies all available rat colonies at Berkeley had large numbers of animals suffering from this disorder.

The retained material in the lungs was presumably Yttrium, Zirconium, Columbium, Ruthenium, Cerium, Praseodymium, Cesium, and probably UX_1. Subsequent studies have shown the first six elements to be retained in the pulmonary tissue. Zirconium and Columbium are held more firmly than the other four. Barium, Cesium, and Strontium are not retained to a significant degree.

The patchy irregular radio-autographic patterns, which showed the activity to have been held primarily in the alveoli, suggest that when the administered solutions came in contact with the moist surfaces, the radio-elements were precipitated and became fixed upon the surfaces of the cells. The absence of activity in the bronchi suggests that the administered material was caught in the mucous secretion of the bronchial epithelium, removed by ciliary action, and finally swallowed. Removal of the entrapped activity from the alveolar cells by phagocytosis probably did not occur since the deposited particles were presumably of molecular size.

It must be kept in mind that the administered material in all of the intrapulmonary experiments was in the soluble form and under conditions presumably most favorable for absorption. If the inhaled radioactivity should be in another physical form (e.g. deposited on dust particles, fog, etc.) the retention factor will be modified by the behavior in the lungs of the inhaled particles. The possible irritative action of the administered solutions (isotonic NaCl at pH 2.5-2.8 containing the radio-elements) has been investigated carefully and no evidence has been secured that indicates any pathological changes ascribable to the solutions employed in these studies.
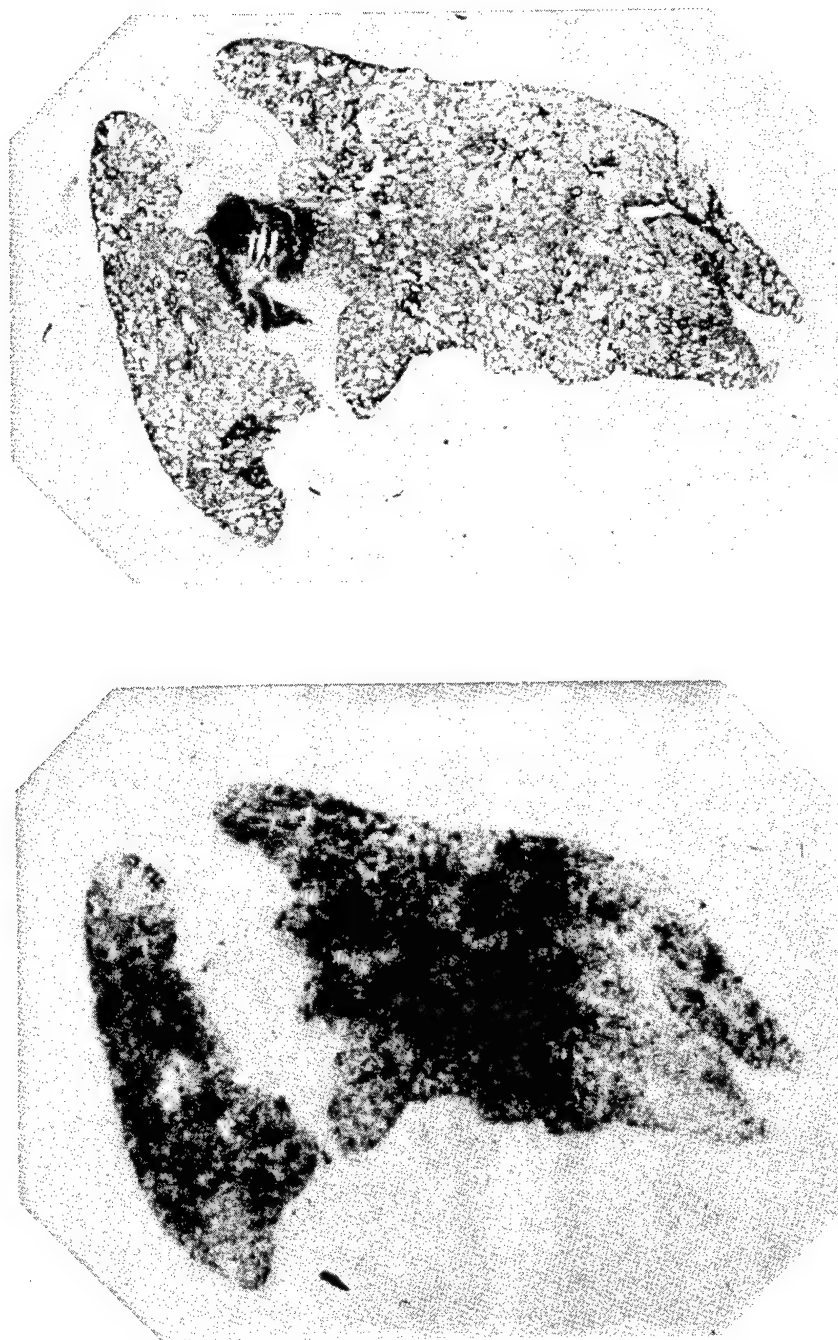
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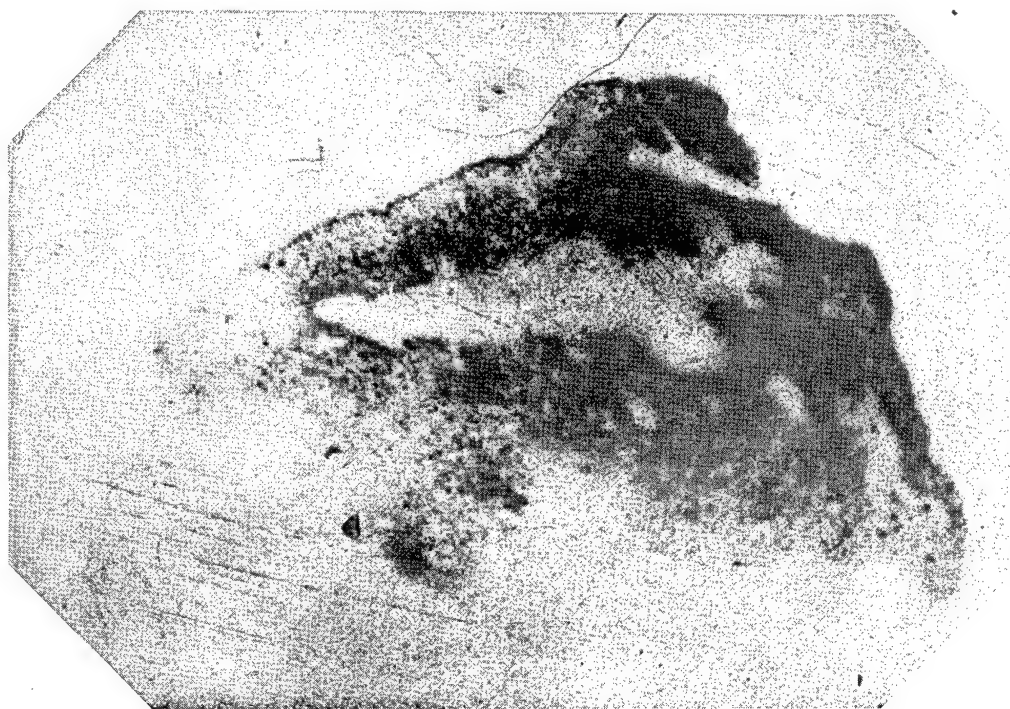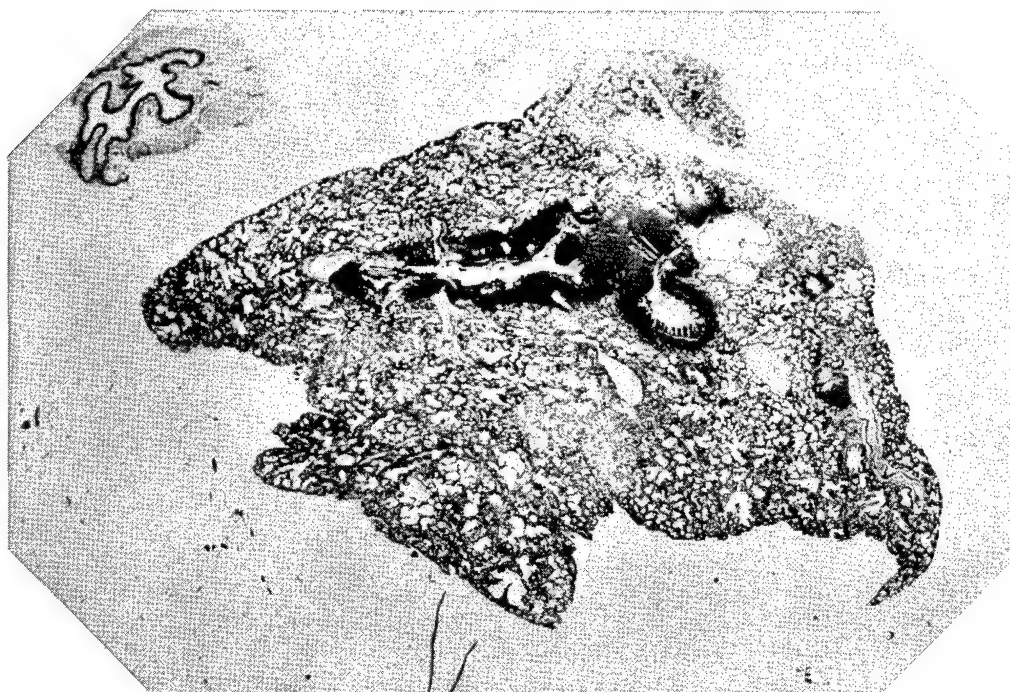Figure 12. Fission mixture. Lung—4 day recovery period (approx. 8×).

Figure 13. Fission mixture. Lung—16 day recovery period (approx. 8×).

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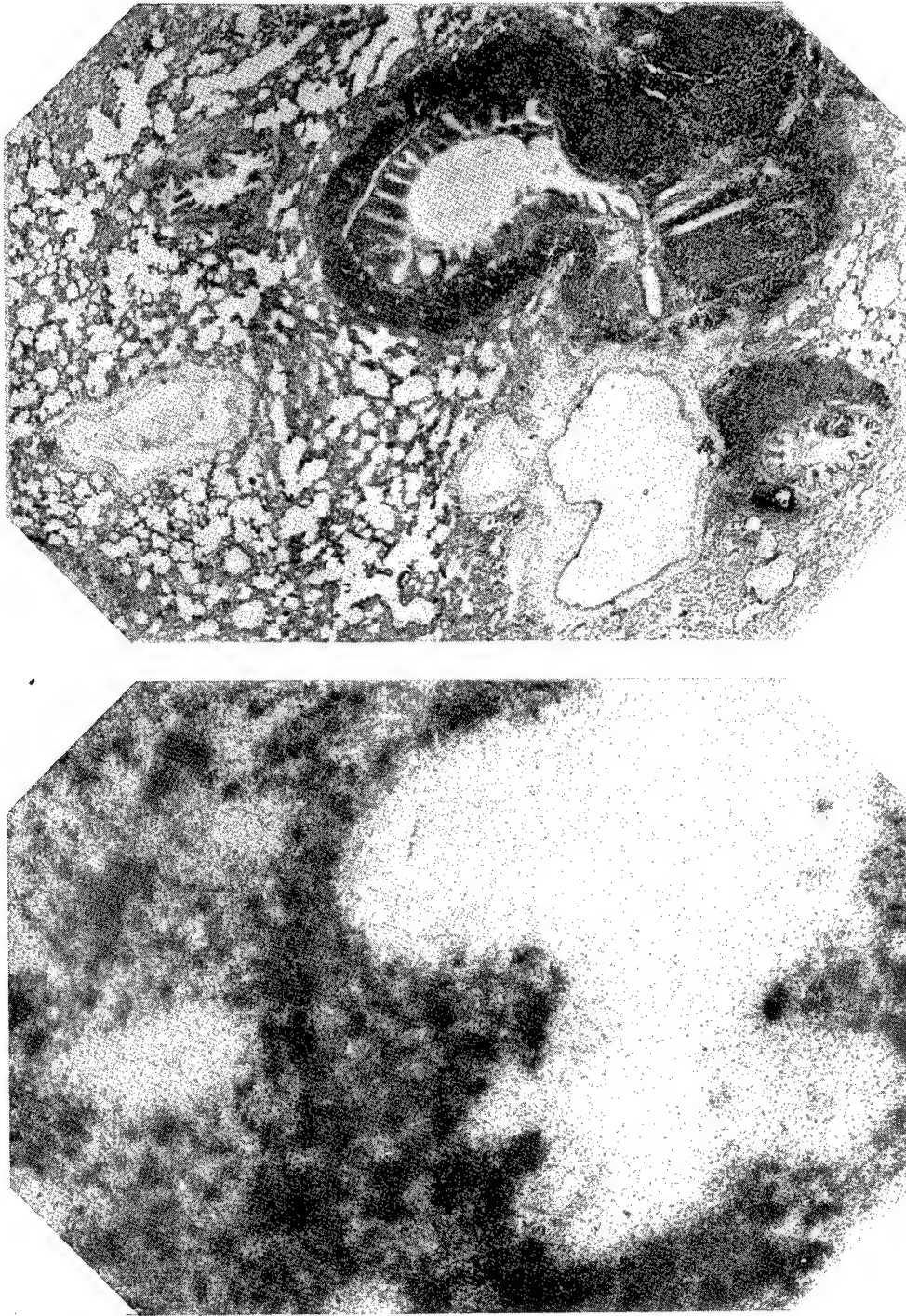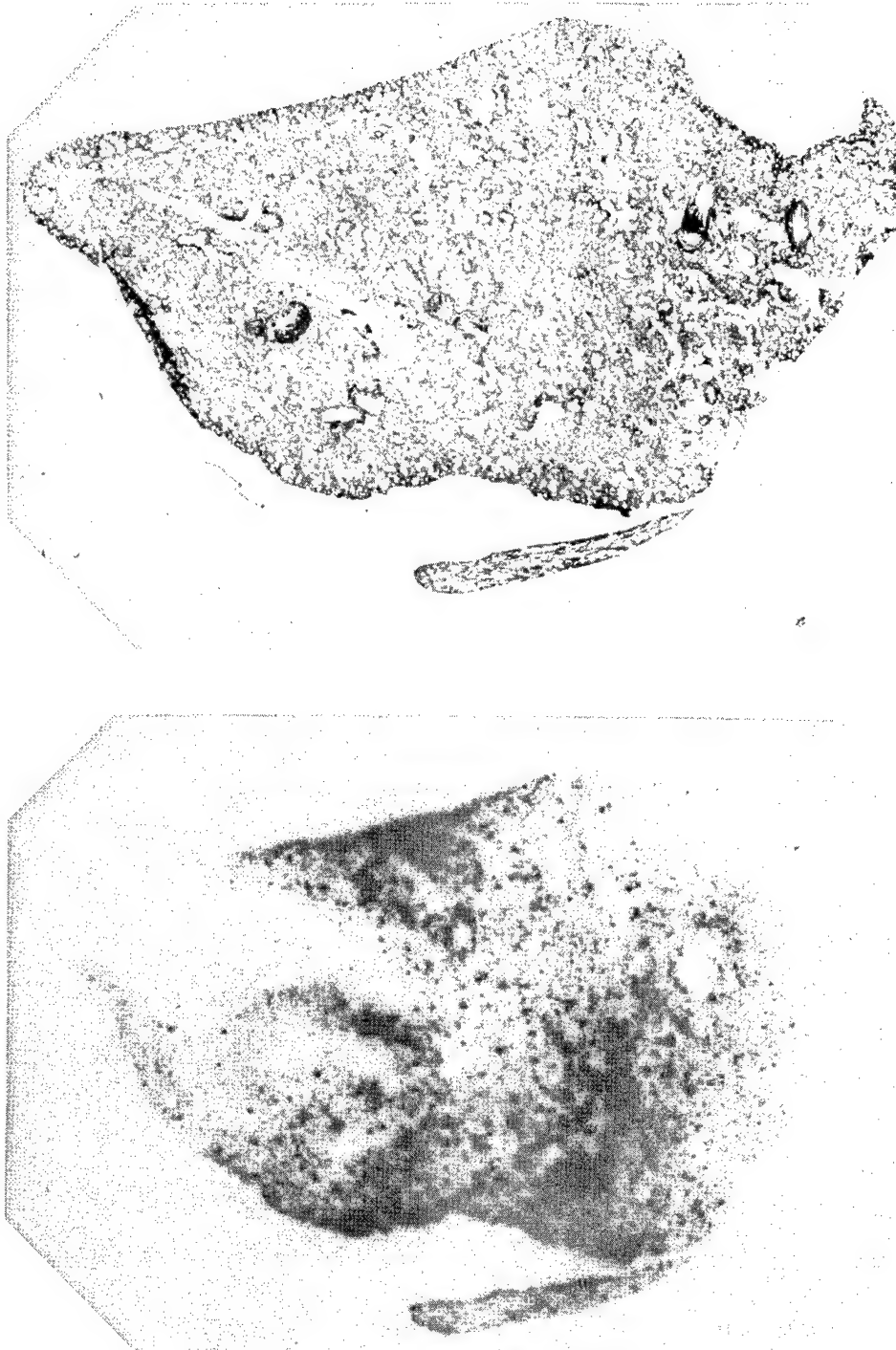

Figure 14. Fission mixture. Lung—16 day recovery period (approx. 31×).

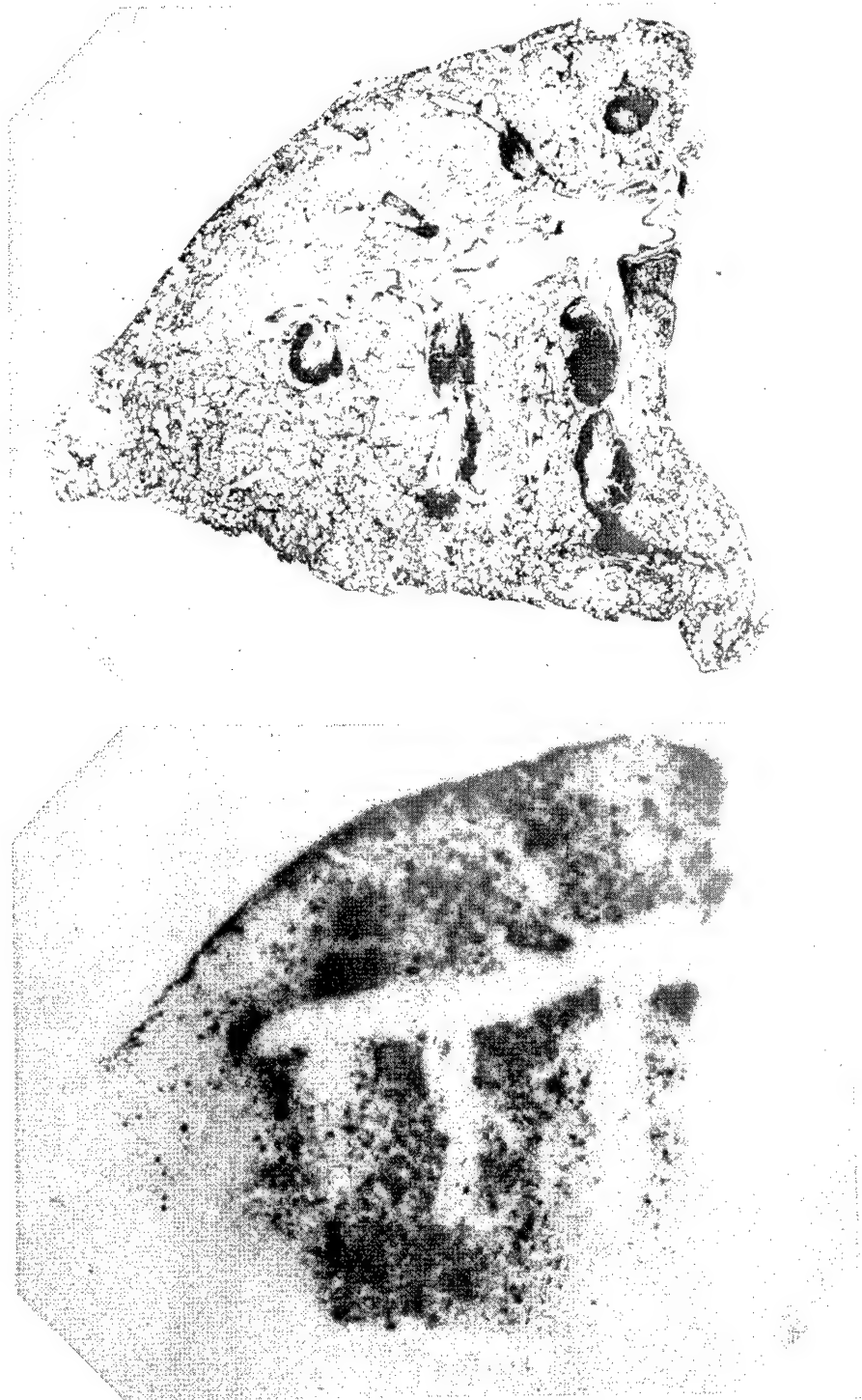Figure 15. Fission mixture. Lung—32 day recovery period (approx. 8×).

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Figure 16. Fission mixture. Lung—64 day recovery period (approx. 7×).

2. Radio-Ruthenium $Ru^{>105}$

Methods: Radio-autographs of pulmonary tissues were prepared from the four, sixteen, thirty-two, and sixty-four day lung experiments. Representative photomicrographs from this series are shown in Figures 17-21.

Results: The four and sixteen day specimens presented radio-autographs which very strikingly duplicated the alveolar patterns of the sections. This effect was markedly diminished in the thirty-two day and sixty-four day lungs. No significant deposition in the bronchial tree, blood vessels, or lymphoid tissue took place.

Discussion: The form in which the $Ru^{>105}$ was retained is open to speculation. The $Ru^{>105}$ was administered as $RuCl_4$ without carrier. It would appear possible that much of the Ruthenium may have been reduced to Ru^0, although the apparent rate of absorption from the lungs seemed far too rapid for metallic Ruthenium if we can use the example of the prolonged retention of metallic silver in Argyria as a guide.

It may prove desirable to study the retention of Ruthenium in the lungs following the inhalation of RuO_4 vapor since its behavior may be quite different from Ru^{++++}.

3. Neptunium(Np^{238}, Np^{239})

Method: Radio-autographs of pulmonary tissues were prepared from the one, four, and eight day lung experiments. Representative photomicrographs from this series are shown in Figures 22-24.

4. Discussion and Results

The radio-autographic pattern showed some tendency to follow the alveolar pattern of the sections but not to the same degree as was noted for Ru^{105}. The other pulmonary structures did not apparently retain significant quantities of Neptunium.

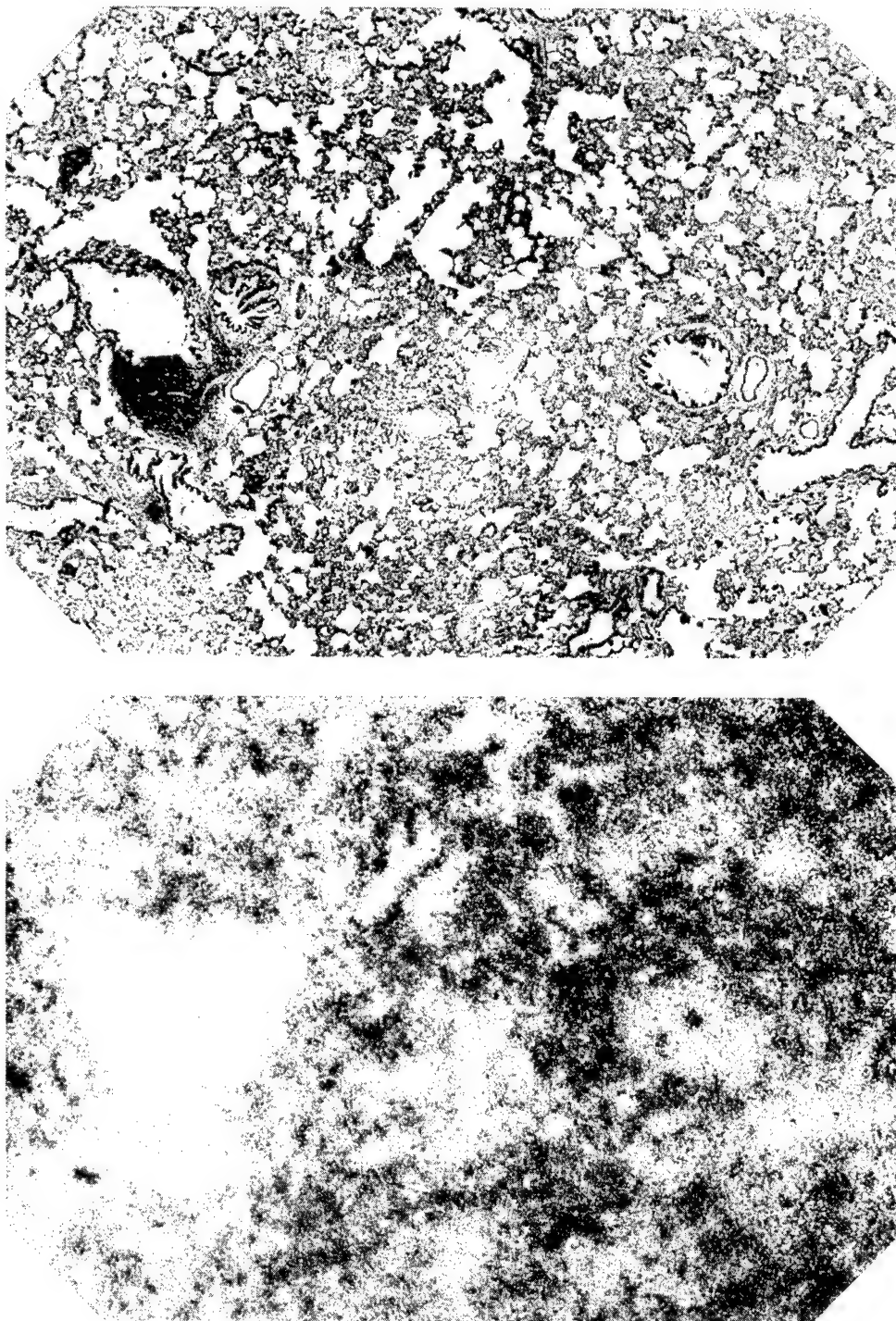Figure 17. Ruthenium. Lung—4 day recovery period (approx. 8×).

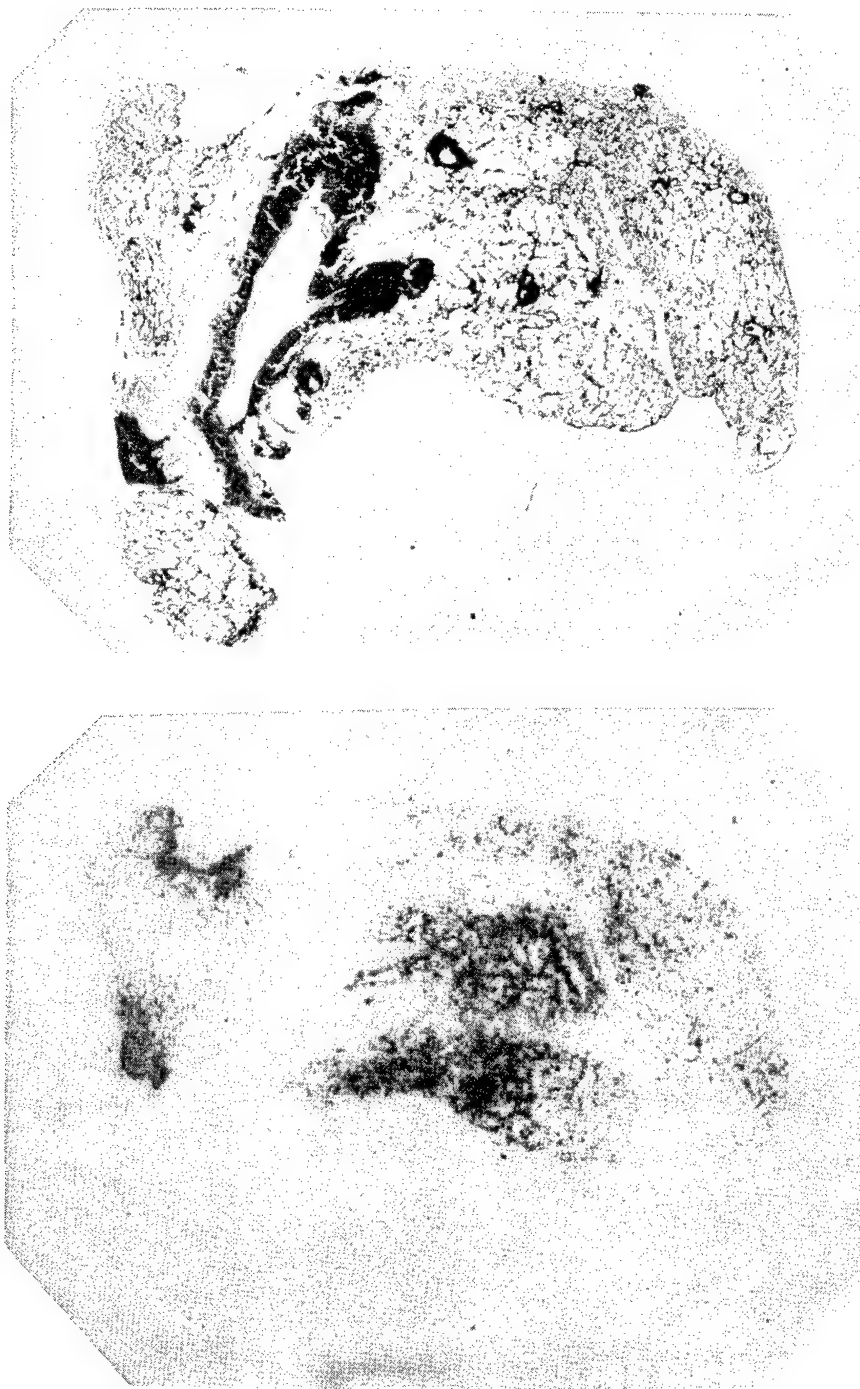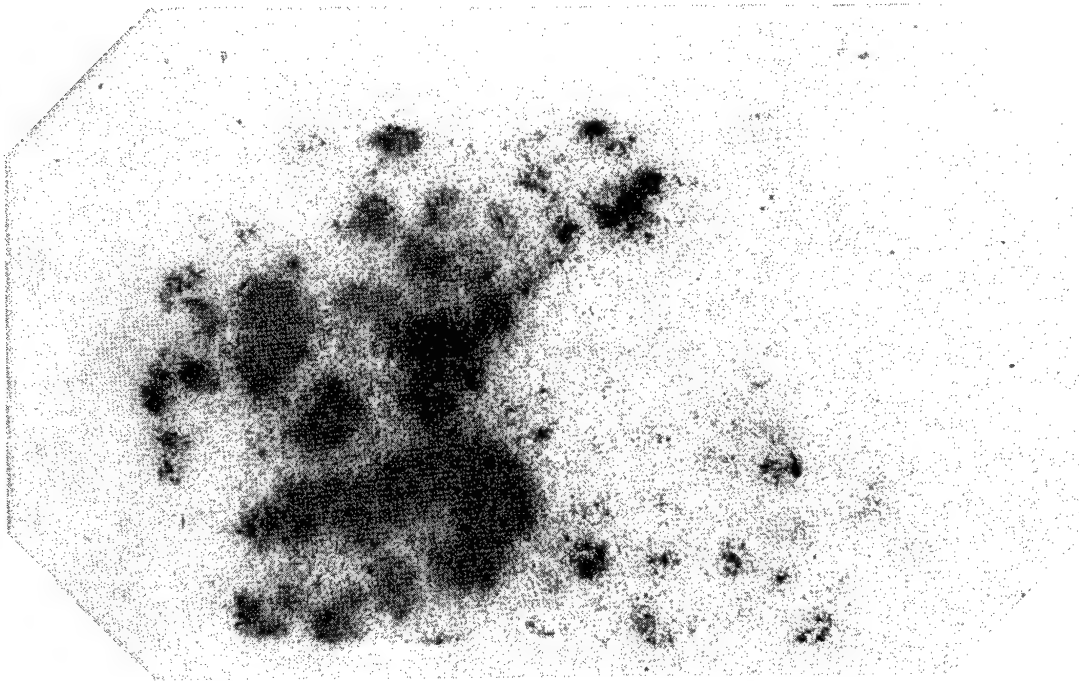Figure 18. Ruthenium. Lung—4 day recovery period (approx. 32×).

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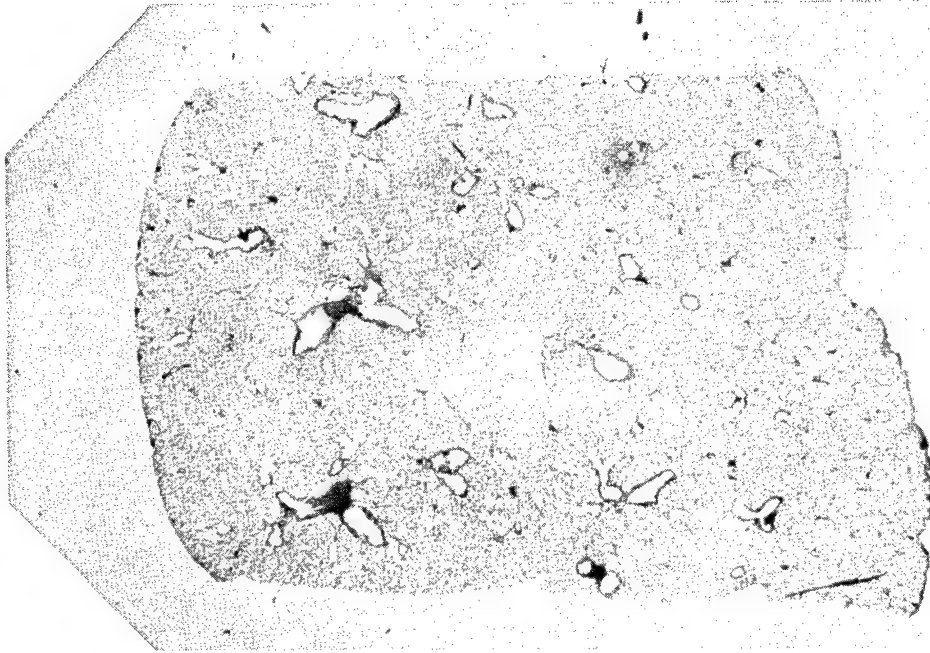Figure 19. Ruthenium. Lung—16 day recovery period (approx. 8×).

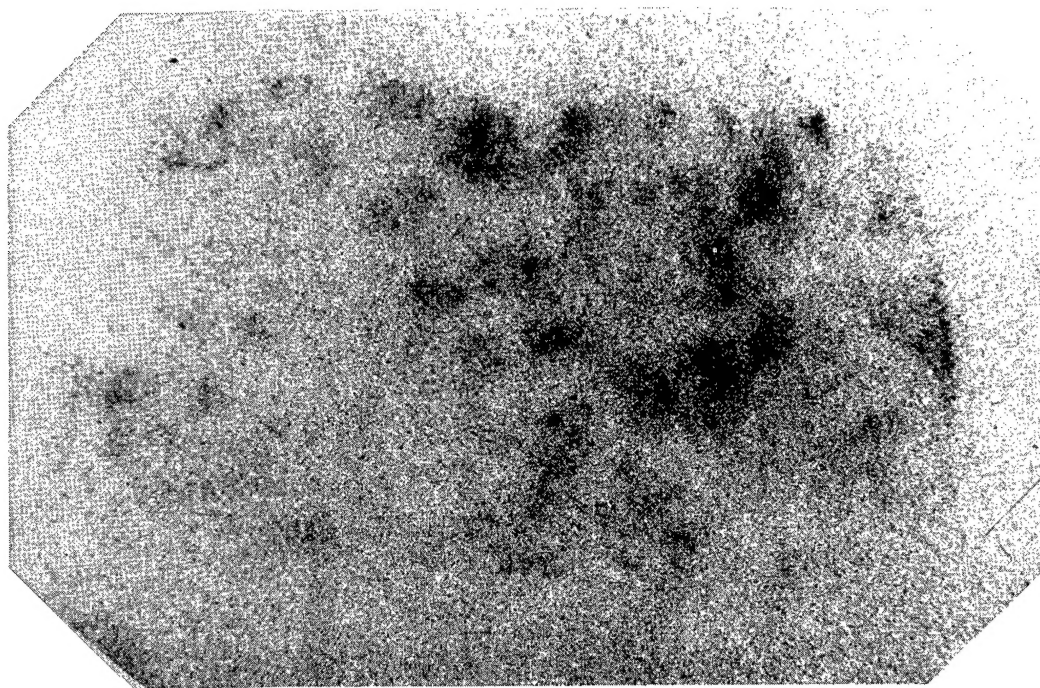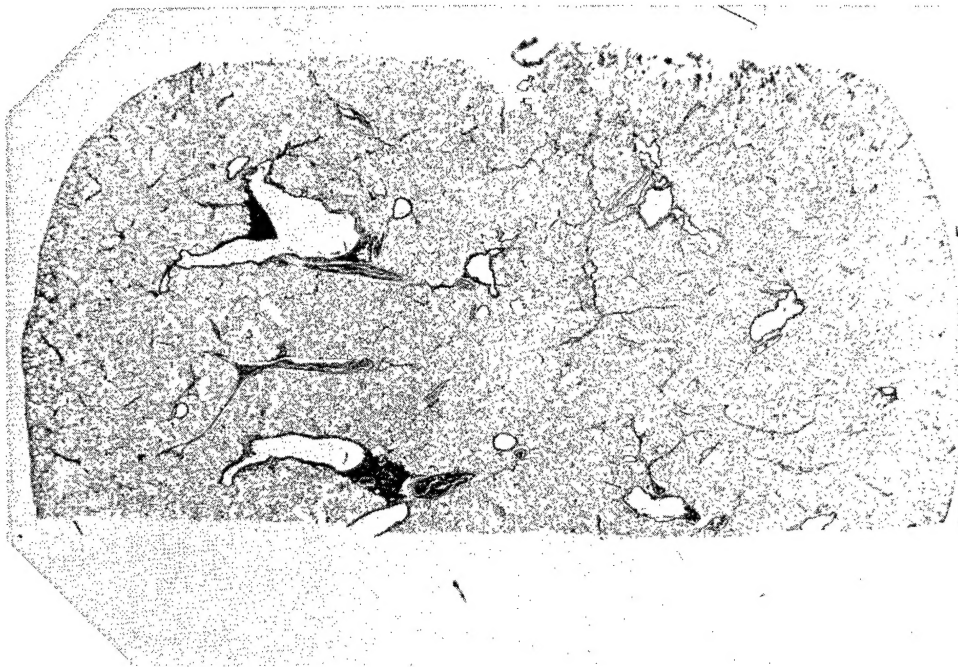Figure 20. Ruthenium. Lung — 32 day recovery period (approx. 8×).

Figure 21. Ruthenium. Lung — 64 day recovery period (approx. 9×).

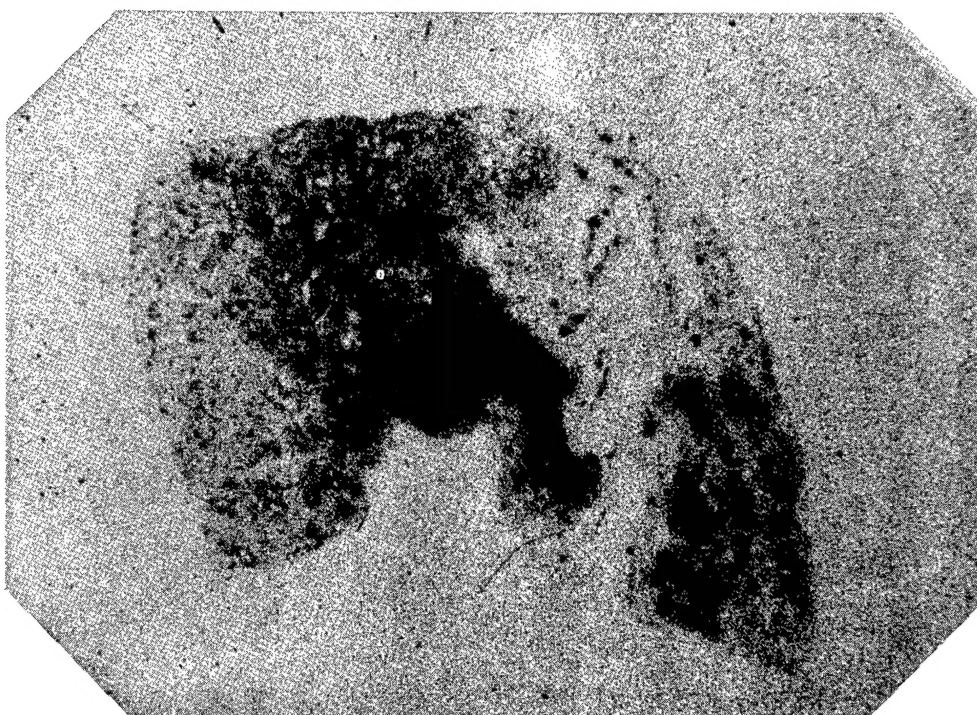Figure 22. Neptunium. Lung—1 day recovery period.

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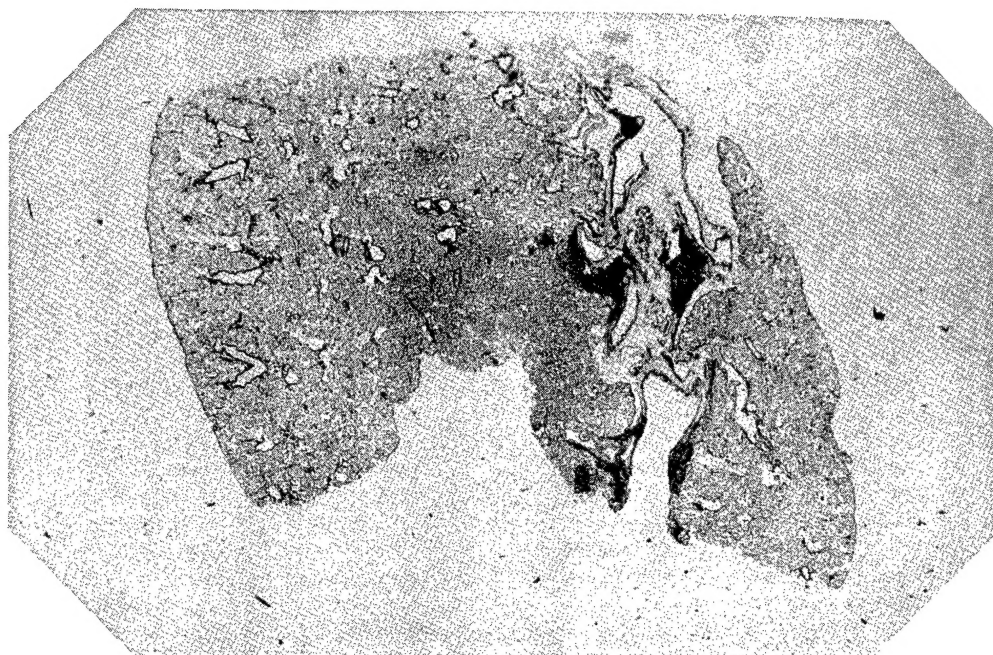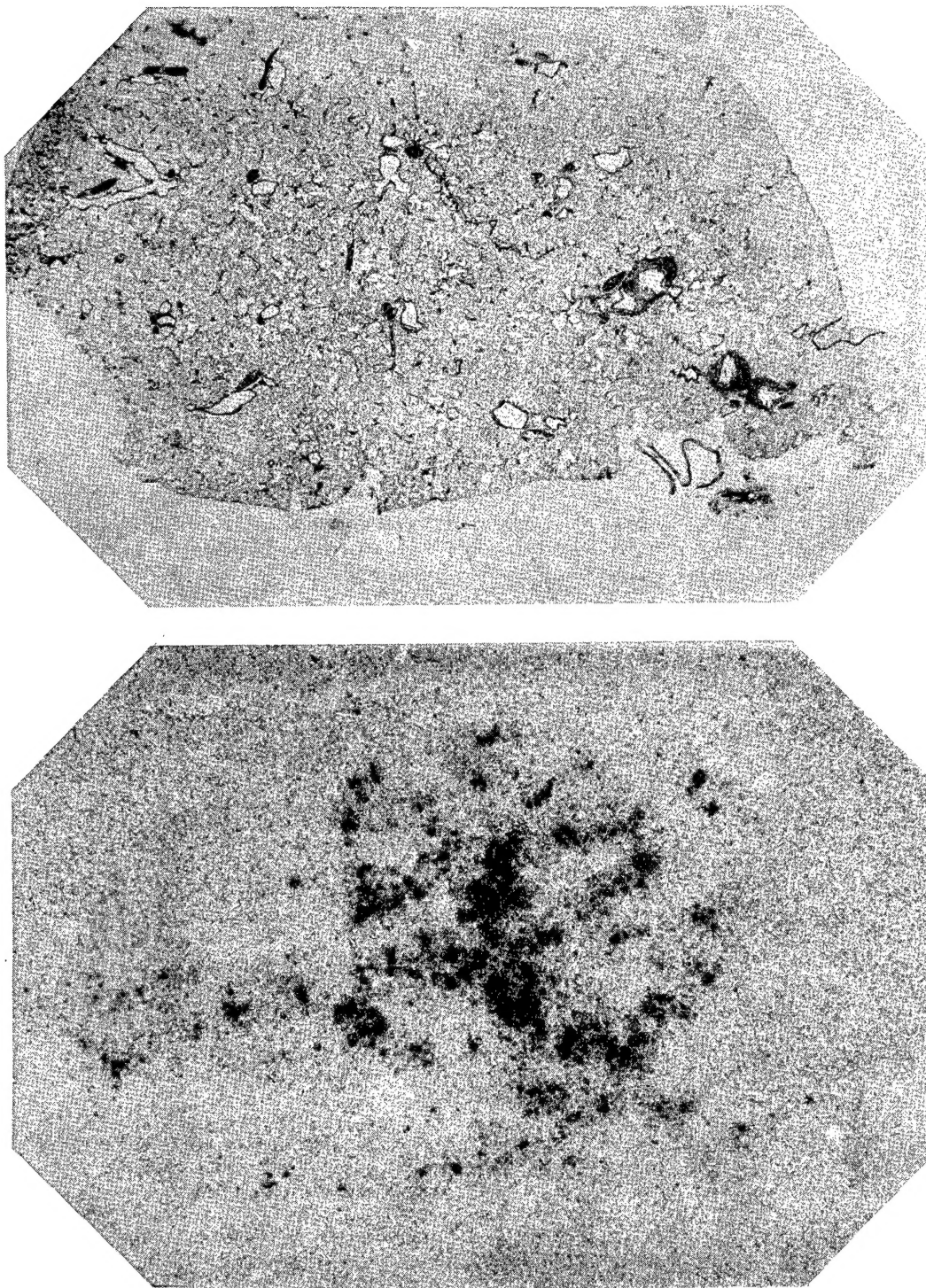Figure 23. Neptunium. Lung—4 day recovery period.

Figure 24. Neptunium. Lung — 8 day recovery period (approx. 8×).